THE American Journal OF Gastroenterology

VOL. 26, NO. 4 OCTOBER, 1956

Radiological Aspects of Gastric Lesions Prolapsing into the Duodenal Bulb

Changes in the Gastrointestinal Tract in Scleroderma and other Diffuse Connective Tissue Diseases

The Indications for Colostomy

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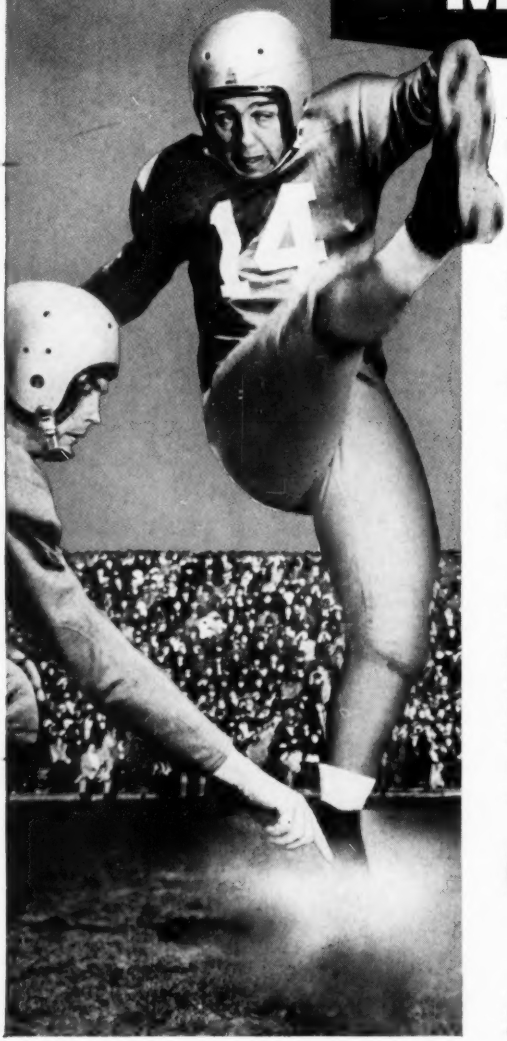

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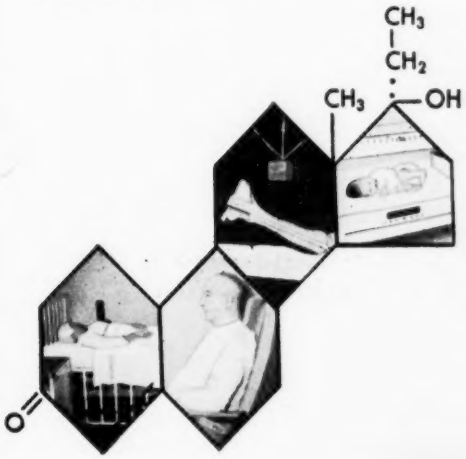

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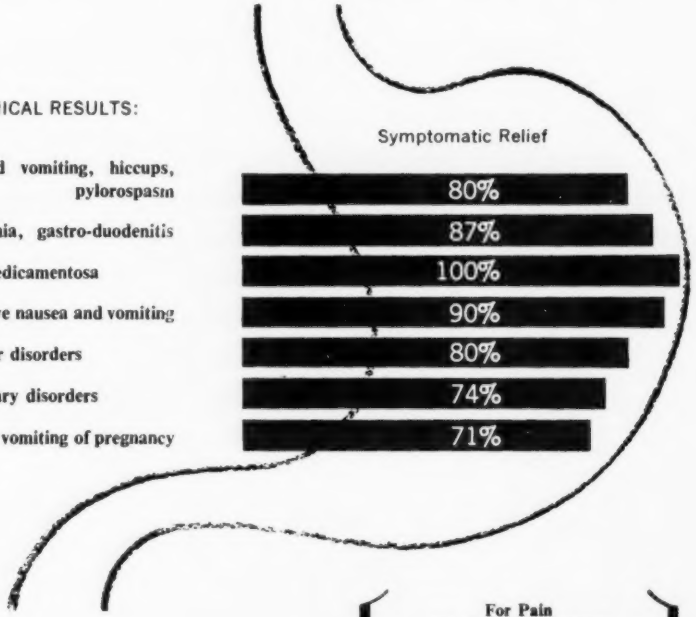

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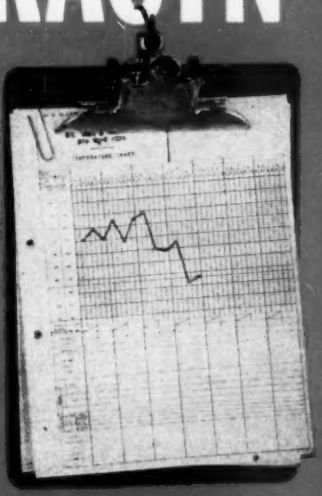

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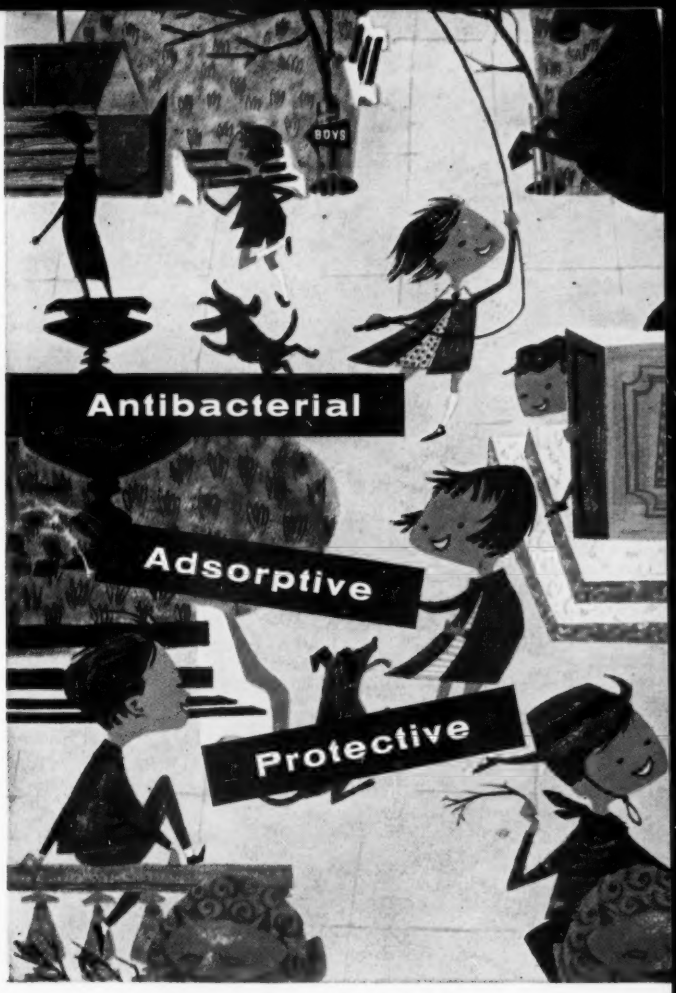

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RADIOLOGICAL ASPECTS OF GASTRIC LESIONS PROLAPSING INTO THE DUODENAL BULB*

ABRAHAM MELAMED, M.D.

Milwaukee, Wisc.

Transpyloric mucosal prolapse, the most frequent form of prolapsing lesion of the stomach, was first reported by Schmieden in 1911. This was regarded as a rather infrequent x-ray finding. Re-evaluation of this condition in the past 10-15 years, however, has shown that mucosal prolapses are found in about 5-10 per cent of all upper gastrointestinal examinations. Based on incidence alone, the entire group of prolapsing gastric lesions is of more than passing interest in the differential diagnosis of upper abdominal disorders.

The x-ray detection and demonstration of prolapsing lesions are largely dependent on the technics employed. Brief discussion of the essential technical features is pertinent. For obvious reasons, recumbent studies in the right anterior oblique and right lateral positions are the most important. In these positions the force of gravity is utilized to induce or facilitate prolapse if such predisposition exists. Eight to twelve serial radiographic views taken in fairly rapid sequence are indispensable in the analysis of any gastroduodenal junction. Even under such circumstances there are instances when only one (Fig. 1) or none[1] of the serial views disclose the prolapse. As an example of the latter, prolapsing mucosa was discovered during surgical exploration a few months following x-ray examination. The x-ray examination should also include fluoroscopy in the upright and recumbent positions, mucosal, spot, compression, posteroanterior and Hampton position views. In our opinion, mucosal prolapses demonstrated by compression alone are of doubtful significance.

There are conflicting statements in the literature concerning gastric emptying in the presence of prolapsing lesions, particularly of the mucosal variety. We believe that the ball-valve mechanism of prolapsing lesions as it affects

*Presented before the Course in Postgraduate Gastroenterology of the American College of Gastroenterology, Chicago, Ill., 27, 28, 29 October 1955.

From the Department of Radiology, Evangelical Deaconess Hospital, Milwaukee, Wisc.

emptying of the stomach should be tested with a meal composed of food and barium sulfate. Results obtained with a plain barium meal may be misleading.

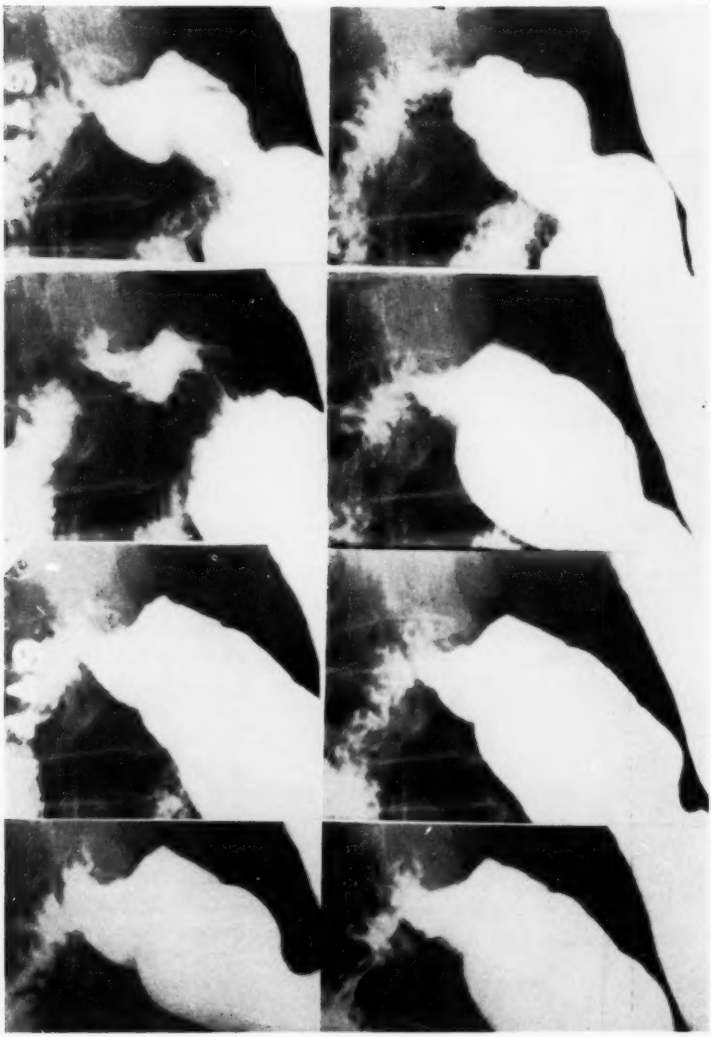

Fig. 1—Prolapsing mucosa visible in only 1 of 8 serial views of the pyloroduodenal junction.

We are all prone to place greater emphasis than we should on opaques for x-ray study of the gastrointestinal tract. The potentialities and possibilities of

plain film radiography of the abdomen have as yet not been exhausted. A conscientious analysis of soft tissue densities and shadows will often obviate the necessity for opaque or other studies. This can lead to a more intelligent approach to diagnostic problems in the abdomen. To the best of our knowledge prolapsing gastric lesions have not heretofore been detected on plain films. We have encountered 3 cases in which such evidence is present; in 1 patient the diagnosis was recognized before the opaque meal examination. It is conceivable that under favorable circumstances such prolapses might be visible in profile, but visualization in our cases was predicated on the presence of gas in the duodenal bulb and projection of the prolapsing mass on end (Fig. 2). The prolapsing tissue appears suspended in the duodenal gas bubble. The lumen of the prolapsing mass is broadened and wavy, conforming to the contour of the mucosa. The outer contour of the mass may be circular or ovoid, but smooth.

Fig. 2—Mass of prolapsing mucosa (arrows) contrasted against gas shadow of duodenal bulb.

The barium meal criteria of the most frequent form of prolapsing lesions are well established. Prerequisite for such a diagnosis is the demonstration of rugae extending into the doudenum. The classical or pathognomonic defect produced in the duodenum is mushroom- or umbrella-like (Fig. 3). The configuration of the defect will vary, however, depending on the number and structure of the redundant rugae. If edema of the mucosa is great, the filling defects will be polypoid instead of corrugated-like. Associated abnormalities of mucosal prolapses are abnormal rugal formation in the antrum, antral hyperperistalsis, widening of the pyloric canal, and in rare instances, ulcers in the prolapsing membrane.

Bleeding is not infrequently reported in association with prolapsing lesions. It is reasonable to suspect that the blood supply of a prolapsing mass or mucosa is compromised to a lesser or greater extent, depending on the caliber of the pyloric canal, degree of pyloric hypertrophy, constancy of pyloric contraction, size of prolapsing mass and reducibility of the prolapse. Our first patient[2] was almost exsanguinated as the result of profuse hemorrhage from 2 large

craters in the markedly edematous prolapsing mucosa. The craters were located at the points where pyloric constriction was greatest and probably prolonged. In another patient, an ulcer crater was visible in the stomach when the prolapsing mucosa receded. The crater was faintly visible in the duodenum when the prolapse was at its maximum. Awareness of the possibility of visualizing such ulcers might lead to the demonstration of greater numbers.

Transpyloric mucosal prolapses may occur as independent entities or secondary to or associated with other local or generalized disease states. In some instances mucosal prolapses represent reversible or irreversible complications of other diseases. We believe that sufficient information and evidence

TABLE I

TRANSPYLORIC MUCOSAL PROLAPSE

1. Primary. Hypermobile and/or redundant rugae
2. Secondary
   - A. Benign
     1. Inflammatory
        - a. Peptic ulcer
        - b. Hypertrophic gastritis
        - c. Antral gastritis
     2. Submucosal edema of stomach
        - a. Congestive heart failure
        - b. Hypoproteinemia; reversal of albumin/globulin ratio
     3. Miscellaneous

        Vitamin B deficiency (?); Pernicious anemia (?); Idiopathic pyloric hypertrophy (?)
   - B. Malignant
     1. Carcinomatous degeneration (Rubin)
     2. Lymphatic leukemia (?) Lymphoma (?)

have been accumulated to enable us to classify mucosal prolapses (Table I). Such classification might assist us in resolving problems concerning etiology and therapy. It is not implied that all mucosal prolapses can be classified at this stage of our knowledge. As more data are accumulated, our understanding of this and related abnormalities will be clarified. It should be added that the etiology of some prolapses can be established if one is given the opportunity to re-examine patients at regular intervals, sometimes extending over a period of months or years. One example will suffice. Prolapsing mucosa is exhibited in a patient about 6 months after the original demonstration of a gastric ulcer. The gastric ulcer failed to heal completely or recurred in the interval between examinations. Examples such as this lead us to believe that many common denominators exist in the gastritides, peptic ulcer and mucosal prolapse.

In this brief presentation it is impossible to consider all types of mucosal prolapses. To demonstrate reversibility of prolapses we have chosen patients in congestive heart failure[3] and in hepatic degeneration. Moderate to marked mucosal slipping is shown during the phase of cardiac decompensation. Disappearance of the prolapse is noted 4 months later when the patient is compensated. The postmortem specimen of a patient who died in congestive heart disease[3] is shown for correlation with the x-ray appearance in the preceding patient. This specimen shows the gross pathological changes that might occur in congestive gastritis. Rugal edema and redundancy are marked. A longitudinal section shows the relationships of the edematous gastric fold to the pyloric ring and duodenum.

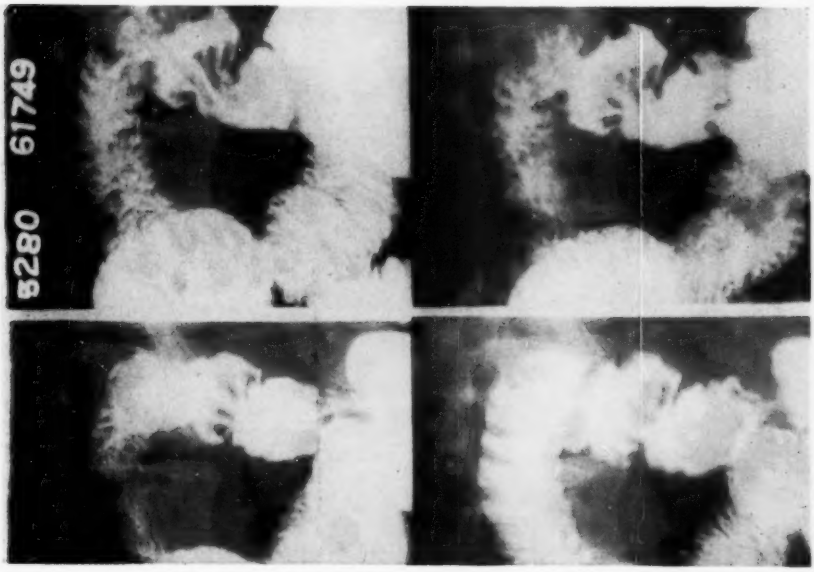

Fig. 3—Classical mushroom-, or atomic bomb-like appearance of transpyloric mucosal prolapse.

Alteration of blood protein levels might also result in mucosal and submucosal edema and slipping of the mucosa. We have found such slipping in several such patients, but in only 1 were we able to follow the patient adequately. The albumin/globulin ratio in this patient with hepatic cirrhosis was 4.45:5.0:(.89:1) 2 days prior to the first x-ray study. Three days before the second examination the ratio was 4.79:3.65:(1.31:1); the mucosal prolapse was hardly perceptible. About 9 months later no prolapse was demonstrable in 2 sittings one week apart. At this time the A/G ratio was 5.59:3.50:(1.6:1).

We have observed mucosal prolapses in patients with lymphatic leukemia, lymphosarcoma, and pernicious anemia. The association was presumably coincidental.

The roentgenographic differentiation between carcinoma of the stomach and mucosal slipping is on occasions quite difficult. In any event, one should make certain that a neoplasm of the stomach is not being overlooked in the presence of the more obvious slipping mucosa. If differentiation between pure mucosal prolapse and carcinoma is involved the problem can usually be resolved by observing the character of the mucosa and distensibility of the segment.

When the prolapse is quite pronounced causing tugging of the wall of the stomach, diagnosis is made more difficult. Such tugging or mucosal intussusception results in a collar-like narrowing, simulating an annular constriction. Postmortem examination of the same case a few months later disclosed no neoplasm. Irregular rugal formation can be misinterpreted to represent carcinoma as exemplified in the next case which came to our attention several years after a diagnosis

Fig. 4—Stages of prolapse of benign gastric polyps into the duodenum.

of cancer of the stomach. Exploratory surgery in 1943 revealed no abnormality. Films taken in 1943, although unsatisfactory, show abnormal rugal formation. Our studies made 5 years later in 1948 revealed prolapse for which partial gastrectomy was performed and rendered complete relief from symptoms including bleeding.

Polyps of the stomach not infrequently prolapse into the duodenum and might produce intussusception. When filling defects are found in the duodenum one's curiosity should always be aroused as to the origin. For this reason it is imperative to re-examine such patients, even if it is for the purpose of ruling out pseudo-tumors such as gas or food. The next case illustrates benign gastric polyps in different phases of prolapse. The serial views were assembled from films obtained during 2 examinations a few days apart (Fig. 4). When pedunculated outgrowths cause intussusception a different picture is produced. Drs. J. Shaiken and M. Moel have kindly provided an example of a malignant polypoid mass which prolapsed as far as the third portion of the duodenum (Fig. 5).

The opacified narrow spaces between the invaginating mass and duodenal sheath result in curvilinear or spiral-like shadows. The intussusception also produces shortening and a funnel-shaped deformity of the stomach.

Other causes of duodenal bulb filling defects or prolapse-like lesions are hypertrophy of the pylorus, enlargement of Brunner's glands, benign duodenal tumors and varices, pseudo-tumors associated with peptic ulcers, duodenal diverticulum adherent to the wall of the duodenal bulb, gallstone impacted in wall of the duodenal bulb. A few examples of such lesions will be presented with a word on differential diagnosis. Concentric hypertrophy of the pylorus will cause a smooth indentation of the base of the duodenal bulb in contrast to the wavy defect of mucosal prolapse. An eccentric indentation of the base of the bulb is created if the hypertrophy is confined to one side of the pylorus. Leiomyoma gives rise to an intramural defect indistinguishable from the latter.

Fig. 5—Intussusception of stomach secondary to prolapsing malignant polypoid carcinoma of stomach. (Courtesy of Drs. J. Shaiken and M. Moel)

Other signs of pyloric hypertrophy as listed by Kirklin and Harris are gastric hyperperistalsis and dilatation.

Enlargement of Brunner's glands cannot always be confirmed microscopically, but the x-ray appearance is quite distinctive. Small constant polypoid filling defects of varying size might simulate prolapse of edematous gastric mucosa when these conditions occur separately. But other signs of mucosal slipping such as rugae in and widening of the pyloric canal are absent. An unusual large solitary adenoma of Brunner's glands is presented as a filling defect similar to those produced by lipoma, neurolemmoma, and other benign tumors of the duodenal bulb as well as pseudo-tumors. An example of the latter occurring in association with peptic ulcer is shown. Irregular scarring and retroactive changes secondary to chronic inflammation can cause bizarre patterns so as to simulate neoplasms.

Summary and Conclusions

Gastric lesions prolapsing into the duodenum exhibit unique features by virtue of their variable nature. For this reason certain technical aspects are stressed, particularly the necessity for obtaining serial radiographic views of the outlet of the stomach.

The plain and opaque meal film criteria of gastric lesions prolapsing into the duodenum have been described. The diagnosis of these lesions can be established quite accurately by x-ray examinations.

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HEREDITARY TELANGIECTASIA COMPLICATED BY A DUODENAL ULCER*

BENJAMIN O. MORRISON, M.D.

New Orleans, La.

Hereditary telangiectasia, known as Rendu-Osler-Weber disease, is a well-defined but rare condition. Characteristic features are aggregations of small blood vessels which become dilated and gradually increase in size. They are apparent most frequently over the skin of the face, arms, and mucosa of the nose, mouth, and pharynx. These lesions are recorded as rarely occurring in the bronchial tree and bowel[1]. These vascular defects are not apparent at birth but develop during middle life. The constituent vessels are superficial and are formed by a single layer of endothelium. Hemorrhage is the outstanding clinical feature. Frequent hemorrhages cause a normocytic hypochromic anemia. Epistaxis is a common presenting symptom. A familial incidence has been shown; the trait is inherited as a Mendelian dominant.

Interest has been aroused in the hematology of this condition by Penfold and Lipscomb's[2] report of a family in which hereditary telangiectasia was associated with elliptocytosis of the red cells. Elliptocytosis is a feature of primary marine vertebrates and these authors put forward an interesting hypothesis that both abnormalities represent a harking back to an amphibious ancestor in which skin and oronasal mucosa have a respiratory function and are therefore highly vascular.

Another recent report[3] describes a family affected by hereditary hemorrhagic telangiectasia in which all three cases examined had a strongly positive tourniquet test.

Shepherd[4] reviewed 25 cases of Rendu-Osler-Weber disease that were reported in the literature from the first case in 1876 to the present time. He found widespread anomalies as part of the generalized vascular dysplasia. In his report 3 cases were found to have the following anomalies: one with telangiectatic hypertrophy complicated by intestinal lesions; one with multiple ileal angiomatous tumors causing severe bleeding; and one with lymphangiomatous tumor of the stomach.

Zabludovich and Acebal[5] reported 3 cases. One was diagnosed by endoscopy of the stomach as being characteristic of telangiectasia; nasal and oral telangiectasia were visualized in the other two.

Another case reported by Rumball[6] was characterized by hematemesis. In addition the patient had large spider angiomata of the face. Gastroscopic

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examination revealed several raised angiomatous lesions along the greater curvature.

Kushlan[7] reported that rutin and hesperidin were used in cases of telangiectasia and proved of value in the presenting hemorrhage. Vitamin C is reported to be without specific effect. Ferrous salts to combat iron deficiency anemia is indicated. According to Cope and Grover[8], however, rutin and a low sodium diet are indicated in treatment. Recently favorable reports were given of the use of rutin.

In the past nasal caustic sclerosing solutions, such as quinine, ethyl carbonate, sodium salicylate and syenosal were employed as reported by Koch et al[9]. Surgical amelioration was directed towards ligation of external carotid artery. Irradiation of the nasal passages has proved ineffective. In 5 cases the tendency to bleed was reduced by estrogen therapy. This might indicate a direct effect on the vascular structure and suppress a lack of estrogen. Estrogen therapy has been effective in controlling nasal hemorrhage.

Case Report:—I. C. M., age 28, a white male, was seen on 6 March 1952 with the chief complaint of stomach cramps and bleeding from nose and rectum. The cramps had been severe for two weeks. Associated with the cramps was excessive gaseous distention. Abdominal pain never awakened the patient at night; however, he had pyrosis and eructation during day and night. Seven years ago an army physician told him he suffered from Osler's disease and that it was familial. At that time he had bleeding from the bowel.

Past History:—The patient had sustained "coral" poisoning of the foot while in the Pacific serving the Navy. As a child he had had pneumonia.

Family History:—The patient's father and paternal grandfather had a bleeding tendency.

Allergic History:—There was no gastrointestinal allergy, hay fever, or asthma.

Social History:—The patient smoked two packs of cigarettes a day until two weeks before his first visit. He takes an occasional drink. He is a lawyer by profession.

Physical Examination:—Physical examination revealed a well nourished white male weighing 167 pounds. The skin showed areas of telangiectasia of the upper lips, chin, neck, and a slight degree in the hypochondriac region of the abdomen. In these regions the skin was slightly hyperpigmented. Dilated veins and telangiectasia of mucous membranes of the inner aspect of right nostril was demonstrated. Only other findings were slight tenderness on palpation in the left costovertebral angle.

Hospital Course:—The patient was admitted to the Southern Baptist Hospital on 10 March 1952 with the same complaints described above. The gastrointestinal series on 7 March showed a constant filling defect in first portion of the duodenum due to duodenal ulcer and he was started on a Sippy regime. Occasional diverticula were found in the descending and sigmoid colon. Suspecting that with Rendu-Osler-Weber disease there was a hypoprothrombinemia, a prothrombin test was done on 11 March which showed a prothrombin time of 44.4 per cent. On the same day a gastric analysis was done. Examination of stool for occult blood showed faint trace. Because the patient had had a slight hemorrhage on the day of admission, daily injections of hykinone were begun on 12 March. Two days later the prothrombin time had risen to 94 per cent. No episodes of bleeding were noted during the remainder of his hospitalization although he had a nasal hemorrhage the day before discharge. There were no other significant laboratory findings, and no elliptocytosis was noted on morphological study of red blood cells.

Besides hykinone, 10 mg. intramuscularly daily, the patient was placed on Parbexin (Vitamin B-complex); Essenamine (a protein supplement), 2 oz. daily; Rutorbin tablets; and Carmethose (anion exchange resin), 2 teaspoonsful every two hours.

Gastrointestinal hemorrhage has not occurred since his hospital admission, but there has been an incidence of epistaxis once or twice a week. None of the authors cited have used hykinone, but I feel its use was beneficial to this patient.

Since the patient has left the hospital he has had frequent epistaxis, but there has been no epigastric tenderness, cramping, or indigestion. Also, no intestinal bleeding has been demonstrated.

Comment

Hereditary hemorrhagic telangiectasia should be considered in the differential diagnosis of gastrointestinal hemorrhage. The outstanding manifestations are lesions of the nose and rectum with hemorrhage and cramping. When the above named measures and treatment have been instituted with success, endoscopy will further demonstrate massive gastrointestinal hemorrhage necessitating total gastrectomy. Such a case has been reported by Williams and Brick[10].

Summary

A case of telangiectasia complicated by duodenal ulcer has been presented. There had been a paternal familial history of bleeding from the nose and bowel. The patient presented the classifical picture of telangiectasia with lesions of the lips, nose, chin, neck, and abdomen.

During his hospitalization there was melena, epistaxis, and cramping. A course of hykinone was instituted. In addition, he was given Vitamin B-complex, protein supplement, and an anion exchange resin.

Since the patient's discharge there has been no epigastric tenderness, cramping, indigestion, or abdominal hemorrhage; however, there has been frequent epistaxis.

Up to the present time rutin, hesperidin, and a low sodium diet have been credited with producing the most beneficial results. As demonstrated by the case presented, however, I believe hykinone and the supplemental medication employed in this case may prove of value in the treatment of this disease.

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DISCUSSION

Dr. I. Snapper (Brooklyn, N. Y.):—In general, the diagnosis of gastrointestinal bleeding due to Osler's disease, is made too readily, as shown so clearly by Dr. Morrison's case of ulcer of the duodenum.

In most patients with multiple telangiectasis of mucous membranes of mouth and nose who are bleeding from the gastrointestinal tract an ailment other than Osler's disease causes the hemorrhage. Only rarely does the autopsy of a patient with a fatal upper gastrointestinal hemorrhage reveal that multiple widespread telangiectases of the jejunum, occasionally of the anterior portion of the stomach, were the cause of the loss of blood. I fully agree with Dr. Morrison that Osler's disease may be a cause of hemorrhage from the gastrointestinal tract. Usually, however, the source of bleeding is either carcinoma or peptic ulcer which has developed independent of the Osler's disease.

In summary, one should not be too hasty in diagnosing Osler's disease of the gastrointestinal tract.

As far as the prolapse of gastric mucosa into the duodenum is concerned, I will gladly accept this diagnosis if it is made by one of the Melamed family of roentgenologists.

I wish to qualify this statement. Fifty years ago many general practitioners —the generalists of today—performed major operations on the kitchen table, sometimes even successfully. These times are behind us and nowadays nobody —unless specially trained in surgery, would dare to undertake major surgery.

Roentgenology of today is in a state of flux which can be compared with the development of surgery 50 years ago. We all have x-ray apparatuses, we all make our own x-rays. Just as in olden times there were specially trained surgeons, and in addition physicians who performed surgery, just so today there are specially trained roentgenologists, and physicians who have an x-ray apparatus.

Even the non-trained radiologist may discover widespread tuberculosis of the lung, large cancers of the stomach and even of the colon. But we have to remember that radiologic specialists, well versed in special roentgenologic technics, can easily diagnose forms of disease which will escape the non-trained generalist.

Prolapse of the gastric mucosa into the duodenum is a source of frequent diagnostic errors. This anomaly should therefore be diagnosed only by a professional radiologist. One can wholeheartedly agree with Dr. Melamed that the final evaluation whether the complaints of the stomach are really due to this prolapse is a different and difficult problem. In all conditions where there is a tendency to edema, in heart disease, lymphoma, lymphatic leukemia, and many other conditions, prolapse of the stomach mucosa into the duodenum may be present and the complaints of the patient may not at all be caused by the prolapse.

If, of course, as in one of Dr. Melamed's cases, two large ulcers are present within the prolapse or if there is carcinoma in the prolapse, then the reason of the signs and symptoms is immediately clear.

To accentuate the importance of the ulcer and to minimize the influence of the prolapse as the cause of abdominal discomfort, may be the tooting of Gabriel's horn of 40 years ago, but it is still sound medicine.

Dr. Owen H. Wangensteen (*Minneapolis, Minn.*):—Dr. Snapper's discussion of this very difficult subject has been helpful. I have had one distressing personal experience with this unusual type of gastrointestinal hemorrhage. My patient concerned a woman of approximately 70 years, for whom I had done a total gastrectomy a year previously because of portal hypertension and gastric

hemorrhage. When bleeding recurred, I went in again. In the terminal ileum I thought I could feel some thickening of the bowel wall. There was nothing to see. I examined all of the intraperitoneal segments of the alimentary canal carefully, inspecting the bowel, running the gut through my hand. The right colon with a modest length of ileum was resected. The pathologist did find a hemangiomatous condition of the ileum in the area where the thickening had been felt. The patient did well for a while but melena recommenced and the patient died. At autopsy, scattered hemangiomatous lesions were quite obvious in the rectum, sigmoid and in the jejunum, which we had failed to find in life. This patient had been proctoscoped many times without a lesion having been seen. It is strange indeed that these lesions may be so difficult to observe during life.

This discussion brings to mind another interesting case which may have nothing to do with this situation. It concerned a young physician's son who was in college. He came to see me with his father. The boy had a waxy pallor; the pulse was feeble and thready, and the boy was obviously on the verge of shock. The hemoglobin was 15 per cent. The only significant finding other than a severe anemia and leukopenia (2,000 W.B.C.) was a persistent melena. The source of the hemorrhage could not be found. After correcting the blood loss, I explored him. Long lengths of small intestine were surrounded by clusters of enormous vessels which crept from the mesentery in claw-like fashion out over the gut. I believed this to be some strange kind of telangiectasis.

Not knowing what better to do, I closed the abdomen and the patient was given x-ray treatment through several portals, omitting a portal on the anterior belly wall to permit reexploration, should that be found necessary. A year or more later, the patient bled seriously again. I failed the first time to determine the portal venous pressure. In fact, I was frightened to even touch the enormous cluster of vessels which surrounded the bowel. What amazed me, on this second exploration, was the absence of the clusters of vessels which had been so prominent previously.

My inference now is that he must have had a period of portal vein obstruction which made those veins so large. By this time, I had had the experience of operating upon several patients with hematemesis in whom no lesion had been found at operation, but for which patients I had performed empiric gastric resection. These experiences had been so satisfactory that with the acquiescence of the patient's physician-father, I did a three-quarter gastric resection. Ten years have gone by since then. The boy remains well. There have been no episodes of hemorrhage. The leukopenia persists. The portal venous pressure was normal in 1945 when I did the empiric gastric resection. I resected the spleen too; it showed nothing of note.

With reference to the paper that Dr. Melamed presented, I have some familiarity with this situation. In fact, long before we knew the entity of

prolapse of the antral mucosa through the pylorus, I had operated upon a few such patients and identified the nature of the situation. We were doing Billroth II operations then for duodenal ulcer—a condition which existed concomitantly in some of these patients.

Under conditions of increased portal venous pressure, this phenomenon, which Dr. Melamed described for us, occurs, I believe, at the esophagogastric juncture. Under the motive force of the increased hydrostatic venous pressure, turgidity of the mucosal folds may occur, I believe. These erectile gastric folds may then project themselves through the esophageal hiatus where the secretion of such fundic gastric mucosa can provoke erosion and hemorrhage. This is a frequent cause of hemorrhage in portal hypertension, I believe.

If an area of gastric mucosa as small as the finger nail is implanted into the esophageal wall, pedicled on its blood supply, an ulcer will develop opposite it in the esophageal wall. Dogs upon which this operation has been done will die of hemorrhage or perforation—even after excision of the remainder of the stomach; so hazardous may be the presence of a small islet of gastric mucosa in the esophagus.

We should divert our notice more frequently therefore to the possibility of projections of gastric mucosa through the esophageal hiatus. How the esophageal hiatus maintains as good continence as it does is really a good question. In patients who complain of heartburn, it is easy usually to demonstrate the regurgitation of gastric juice into the esophagus by passing a nasal tube into the midesophagus. With patients supine or prone, in patients complaining of heart burn, gastric juice can usually be aspirated when suction is applied to such an inlying tube in the midesophagus. We need to devote more study to the manner in which the cardioesophageal sphincter works. It is an important mechanism.

CHANGES IN THE GASTROINTESTINAL TRACT IN SCLERODERMA AND OTHER DIFFUSE CONNECTIVE TISSUE DISEASES*†

FREDERICK D. MALKINSON, M.D.

and

STEPHEN ROTHMAN, M.D.

Chicago, Ill.

The term "diffuse connective tissue disease" has become distinctive for any of those disorders in which the primary pathological features are characterized by systemic alterations in connective tissue. The alterations commonly found in these disorders are mucoid degeneration, reflecting changes in the mucopolysaccharides of the ground substance, and fibrinoid degeneration, apparently resulting from the combination of a tissue or blood protein with mucopolysaccharides derived from ground substance[1,2]. Both types of degeneration may be followed by further changes of hyalinization and sclerosis.

The almost universal distribution of connective tissue and its susceptibility to these abnormal changes in any anatomical situation accounts for the great multiformity of clinical manifestations in this group of connective tissue diseases. It is our purpose here to discuss specifically the symptoms and pathological alterations that may accompany involvement of one such anatomical site, the gastrointestinal tract, and to illustrate these abnormalities by appropriate case material selected from patients with scleroderma, dermatomyositis, and acute systematic lupus erythematodes.

Scleroderma

Over 50 years ago Ehrmann[3] first called attention to gastrointestinal changes in scleroderma when he recorded a case with esophageal involvement. Since that time alterations of the esophagus in scleroderma have been widely studied while more recently descriptions of changes elsewhere in the gastrointestinal tract have also appeared in the literature.

When present, esophageal symptoms usually occur early in the course of the disease and include dysphagia, sensations of presternal burning, fullness, or pain, nausea, and regurgitation. Rarely, esophageal complaints may actually precede the onset of skin changes for periods up to 3 years or more. Not infrequently, where esophageal symptoms are absent altogether, x-ray examination will nevertheless reveal some abnormalities of function.

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†From the Section of Dermatology, Department of Medicine, University of Chicago. (Chief of Service: Stephen Rothman, M.D.)

Recent indirect cinéradiography studies[4] with barium emulsions have shown that disturbances of gastrointestinal function in scleroderma may actually occur at the very beginning of the gastrointestinal tract with the act of swallowing. Impaired deglutition may be demonstrable and is largely the result of incoordination and limitation of the normal movements of the tongue and soft palate, although defective or absent contraction of the pharyngeal musculature is occasionally present. Spillage of food into the trachea, however, has not been observed.

Where early esophageal involvement is present, fluoroscopy[5,6] may show only slight delay in transit of a barium bolus with the patient in a supine position. More advanced peristaltic impairment of the lower two-thirds of the esophagus is reflected in markedly delayed transit time in the upright position. The terminal 2 to 3 cm. of the esophagus may be slightly narrowed with some widening above this point, but complete obstruction is rarely seen. Hiatus hernia resulting from sclerosis and shortening of the esophagus may be visualized[7].

Esophagoscopy[5] may show a thickened wall with flattening of the normal folds in the lower two-thirds of the esophagus, whitish mucosal exudate, mucosal erosions and ulcerations, and fibrous constrictions markedly narrowing the lumen.

Studies of biopsy specimens obtained during esophagoscopy and at necropsy have revealed the chief histopathologic changes in the esophagus[4,8-10] to be patchy hyperplasia of mucosal epithelial cells with interspersed areas of erosions or ulcerations, infiltration of connective tissue with acute and chronic inflammatory cells, sclerosis of the submucosa, varying degrees of atrophy and degeneration of the muscular coats, and fibrosis of the serosal layer. Blood vessels often show inflammatory cell infiltration and thickening of the walls, luminal narrowing or obliteration, and thrombotic occlusion. Such changes may be especially marked at the bases of mucosal ulcerations. The preservation of myenteric plexi in many instances argues against a primary disturbance of the sympathetic nervous system in scleroderma. More likely the pathologic changes represent primary involvement of esophageal connective tissue and, perhaps, muscle fibers which, by consequent impairment of peristaltic movements, indirectly accounts for secondary mucosal and inflammatory changes induced by regurgitation of gastric contents[11].

In the more recent literature attention has also been directed to alterations occurring lower in the gastrointestinal tract in scleroderma[6,8,9,10,12,13]. These changes are found chiefly in the proximal small intestine and in the colon and may or may not be accompanied by abnormalities in the esophagus. The stomach, ileum, and rectum are rarely involved. Anorexia, nausea, vomiting, constipation, and cramping abdominal pains associated occasionally with abdominal distention and, rarely, occult or gross blood in the stools represent the characteristic symptoms and signs. These may in fact comprise the predominant clin-

ical disturbances in advanced or preterminal cases. Although obstruction is not seen, the complication of paralytic ileus has been reported[14].

X-ray examination with barium[6,13,15] may show dilatation of the duodenum and jejunum, while residual pockets of barium persisting up to 24 hours after initial visualization attest to markedly delayed transit time. Small bowel involvement is characteristically patchy but may be diffuse. Abnormalities of the mucosal pattern are not a prominent feature. The large intestine, when involved, shows intermittent areas of sacculation with slight rigidity and narrowing of the intervening bowel segments, the narrowed portions of bowel representing the sites of pathological change. Disturbances in function[9] are related to impairment of peristalsis.

Postmortem examinations in some cases[8,9,10] have revealed peritoneal thickening with visceral adhesions, ascites, pseudodiverticulosis, and mucosal ulcerations. Histopathologic alterations[8,9,10] are analogous to those described for the esophagus, although blood vessel changes are usually less marked.

Case 1:—Mr. J. F., a 48-year old male*†, was first seen at AMBH in 1940 with the complaints of stiffness and swelling of many joints, numbness of the hands, and progressive hardening of the skin over the extremities. At that time the skin changes were consistent with a diffuse scleroderma and pertinent laboratory data were normal. X-ray examination, however, revealed a 42 per cent increase in cardiac size and atrophic and destructive changes in the distal phalanges and wrist joints.

In 1941 bilateral cervical and thoracic sympathectomy failed to alter the course of the disease. Because of progressive dysphagia, esophagoscopy with biopsy and fluoroscopic examinations of the esophagus were performed in 1942. The findings were consistent with sclerodermal changes, and severe lower esophageal stenonis was observed. Thereafter mechanical dilatations gave some symptomatic relief.

In September, 1946, the patient noted the onset of severe cramping abdominal pain in the left lower quadrant associated with marked constipation. Proctoscopy was negative and technical difficulties prevented adequate x-ray examination with barium.

In March, 1947, the patient developed a severe upper respiratory infection with thoracic pain, pulmonary congestion, dyspnea, and abdominal distention. He was hospitalized 5 days later at which time he showed cyanosis, severe dyspnea, widespread thoracic rales, greatly distended abdomen, and edema of the legs. A few hours later he passed a bloody stool and shortly thereafter expired.

*Autopsy and general pathological examination were performed by Dr. C. Lushbaugh.
†Published previously (Case 2, ref. 2; ref. 9).

Gastrointestinal examination:—The esophagus was shorter than normal. Four to 5 cm. of the cardiac portion of the stomach were above the diaphragmatic hiatus. The lumen of the esophagus was constricted by dense fibrous tissue at the esophageal-cardiac junction, and in this same region there was a 2 x 3 cm. ulcer 2 mm. deep. The epithelium of the distal half of the esophagus showed innumerable 3-4 mm. whitened islands separated by deep linear crypts.

The abdominal cavity contained 1,000 c.c. of slightly cloudy, thin yellow fluid. The peritoneum over the gangrenous segment of bowel was opaque and covered by fibrinopurulent exudate.

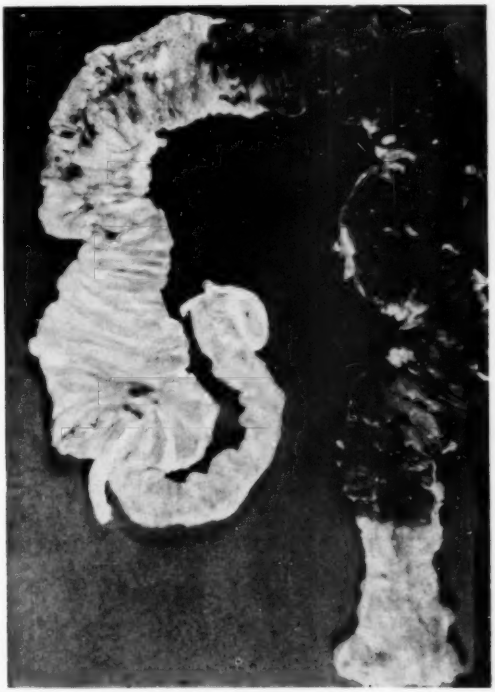

Fig. 1—Case 1. Photograph of the mucosal surface of the terminal ileum, colon, and rectum, showing the edematous, gangrenous segment of bowel and its relatively sharp delineations. (Reproduced by permission of Williams and Wilkins Co., Baltimore, Md.)

The stomach and small intestine were normal in appearance except for small peritoneal hemorrhages over the terminal duodenum.

The ascending colon was normal. The transverse colon contained several small pseudodiverticula. From the splenic flexure to the rectosigmoid junction the bowel was dark red to brown, dilated, and gangrenous (Fig. 1). The epithelium

of this portion of the colon was dark red and edematous, and numerous 3 to 5 mm. sharply marginated ulcers were seen. The rectal mucosa showed 2 ulcerations, the largest 2 x 20 mm., but was otherwise normal.

The left coeliac and sigmoidal arteries and veins and their arcadal communications were occluded by thrombi.

Histopathological examination:—The epithelium of the lower half of the esophagus was thickened. In the floor of the ulcer was a small artery completely obliterated by intimal fibrosis. The muscularis mucosa was atrophic and fibrotic. The submucosa consisted of dense acellular connective tissue. The muscularis was atrophic and partially replaced by dense connective tissue. Many arteries showed intimal fibrosis.

The stomach and small intestine showed some submucosal fibrosis, scattered foci of atrophy and fibrosis of the muscularis, and subperitoneal fibrosis.

In the gangrenous portion of the large bowel (Fig. 2) the mucosa was necrotic or missing. A polymorphonuclear cellular infiltrate was seen in the mucosa and submucosa. The submucosa was thickened throughout. There was marked atrophy and fibrous replacement of the circular muscle layer in the descending colon and sigmoid. The arterial walls showed a polymorphonuclear cellular infiltrate and marked fibrosis, the severest changes occurring at the bases of the ulcerations.

Case 2:—Miss V. S., a 24-year old female, was admitted to AMBH for the 7th time in February, 1955, with a recurrent diarrhea of 7 years duration*†. At the age of 5 years she had had intermittent bouts of abdominal pain without diarrhea which disappeared with a low residue diet. Recurrence of severe cramping pains at the age of 17 was associated with up to 18 stools daily, some of these containing bright red blood. Several months later the patient noted blanching and numbness of the fingers on exposure to cold. Muscle pains and stiffness, dysphagia, arthralgia and arthritis appeared in the following two years and when she failed to respond adequately to ACTH therapy she was hospitalized at AMBH in 1950.

P. E. revealed a smooth, dry, pale skin with tender 3-5 mm. erythematous nodules over the tendons of the metacarpal-phalangeal joints of both hands. There was increased skin temperature over both knee joints. Examination was not otherwise remarkable.

Significant laboratory findings included Hgb. of 10 gm., occasional 4 plus guaiac stools, and plasma protein of 8.4 gm. per cent with 4.4 gm. per cent of albumin and 4.0 gm. per cent of globulin. Barium enema revealed findings

*Autopsy and general pathological examination were performed by Dr. B. Spargo.
†Permission to publish this case was granted by Dr. J. Kirsner.

suggestive of chronic ulcerative colitis and chest films showed diffuse pulmonary fibrosis. Skin and muscle biopsies at that time were not diagnostic.

After numerous bouts of fever and pneumonitis, and the appearance of clinical signs of pericardial effusion, she was subsequently discharged improved on cortisone therapy.

During the next 3 years exacerbations of fever and arthritis continued, poorly controlled by ACTH, cortisone, and phenylbutazone. Joint symptoms

Fig. 2—Case 1. Photomicrograph (x20) of the gangrenous colon showing the necrotic epithelium, edematous fibrous submucosa, thrombosed veins, and typical atrophy and fibrosis of the circular muscle. (Reproduced by permission of Williams and Wilkins Co., Baltimore, Md.)

progressed with limitation of motion in shoulder, wrist, finger, and elbow joints. In 1953 the patient suddenly developed hematemesis and melena. At laparotomy a bleeding duodenal ulcer was found; subtotal gastric resection and anterior gastroenterostomy were performed.

Following discharge from the hospital the patient's course was slowly downhill. Her last admission was in February, 1955, at which time she was

weak and bedridden, severely anemic, and still having 6-7 watery stools daily. Despite blood transfusions, continued adrenal steroid therapy, and antibiotics she developed increasing respiratory distress and expired on the 5th hospital day.

Postmortem examination revealed generalized scleroderma with extensive involvement of the entire gastrointestinal tract, diffuse pulmonary fibrosis, advanced skin and joint changes, and focal endocardial fibrosis.

Gross gastrointestinal examination:—The esophagus showed slight uniform thickening of the wall with several superficial mucosal ulcerations in the distal third.

The lower one-third of the stomach was resected. The gastrojejunal anastomosis was intact. The remaining stomach was grossly normal except for a slightly thickened wall.

The terminal 18 inches of ileum showed a somewhat thickened wall and hyperplastic mucosa with numerous 2-3 mm. superficial ulcerations.

The colon was uniformly involved with narrowed luminal circumference throughout. The wall was diffusely thickened and haustral markings were absent. The mucosa of the entire large bowel was thickened and showed a pronounced granular appearance.

Histopathological examination:—The esophagus showed a thickened mucosa and hypertrophied muscularis mucosa. The *lamina propria* and submucosa were replaced by dense acellular connective tissue. The circular and longitudinal muscle layers revealed areas of focal atrophy throughout, with replacement by connective tissue. The small arteries showed intimal fibrosis and the small veins ectasias.

The stomach, jejunum, and distal ileum revealed changes analogous to those seen in the esophagus.

In the colon the mucosa was hyperplastic and showed a cellular infiltrate in which plasma cells and eosinophiles were prominent. The muscularis was hypertrophic but showed numerous areas of fibrosis. The submucosa was replaced by dense connective tissue and proliferative and degenerative changes of the small arteries were marked. The longitudinal and circular muscle layers showed widespread atrophy and replacement by connective tissues.

Dermatomyositis

Reports of gastrointestinal lesions in dermatomyositis are scarce. Wainger and Lever[16], reviewing the literature in 1949, could find only 9 such recorded cases. In 1952, 3 additional cases in children were reported by Wedgwood et al[17]. The earliest reports regarded the gastrointestinal changes purely as inci-

dental findings and it remained for Karelitz and Welt[17] in 1932 to propose instead that they were an integral part of the diffuse disease process in dermatomyositis.

Where gastrointestinal abnormalities are present in dermatomyositis, associated symptoms may be present or absent. The most common related complaint is that of dysphagia. This appears in many patients, usually unaccompanied by other gastrointestinal disturbances, and has been attributed to primary involvement of the pharyngeal musculature. With involvement elsewhere in the intestinal tract cramping abdominal pains, alternating constipation and diarrhea, vomiting, and occasionally occult or gross blood in the stools have been described.

Fig. 3—Case 2. Photograph of the mucosal surface of the distal half of the esophagus and proximal portion of the stomach showing the deep, penetrating ulcerations in the esophagus and at the cardia.

Clinical evaluation may reveal ulceration of the rectal mucosa[16] on proctoscopy. X-ray examination in 1 patient[16] showed dilatation, gross segmentation, and loss of mucosal pattern throughout the small intestine with delay in transit time.

Postmortem examination[16,18-22] may reveal fluid in the abdominal cavity and a thickened edematous wall in any portion of the intestinal tract. Mucosal petechiae are occasionally seen. In 1 case[22] the gastric mucosa showed numerous ecchymoses with central necrosis while in the lower portion of the small bowel several erosions in the mucosa were present. Mucosal ulcerations, undoubtedly the source of the hemorrhages reported, have frequently been described as an outstanding pathologic feature and have been found from the esophagus to the rectum. The lesions are often numerous, irregular in outline, range in size to 2 cm. or more in diameter, and may be shallow or extend to involve the musculature of the intestinal wall. In one instance numerous perforations were observed[16].

Histopathologic changes[16,19-21] include edema of the intestinal wall and fibrous intimal thickening of many large and medium-sized arteries with resultant narrowing of the lumina. Marked degenerative changes in the musculature of the esophageal wall were described in one case[20]. The areas of mucosal ulceration show extensive hemorrhage, necrosis, and acute inflammatory changes, and often, but not invariably, the small arteries and veins at the bases of these ulcers show intimal thickening and fibrous obliteration of the lumen.

One further significant feature remains to be discussed. New malignant visceral growths occur in patients with dermatomyositis[23,24] more frequently than in the general population and when present are usually detected at some time after the signs and symptoms of dermatomyositis have become apparent. The relationship of the 2 conditions has been reinforced by the observation of clinical improvement in the dermatomyositis in 3 patients following extirpation of the tumor.

By 1952, 21 cases of dermatomyositis and carcinoma had been recorded in the literature. Among these were 1 patient with carcinoma of the esophagus, 5 with carcinoma of the stomach, and 1 with a rectal carcinoma. Adenoid or undifferentiated forms of tumor were the pathological types usually encountered.

It is apparent that routine search for associated malignancy should be made in all patients with dermatomyositis. Since approximately one-third of patients with both conditions have been found to have gastrointestinal tumors, thorough examination of the gastrointestinal tract is a most important feature of the recommended patient survey.

Case 3:—Mrs. R. P., a 50-year old white housewife, entered the AMBH for the second time on January 5, 1955, because of dermatitis and progressive generalized muscular weakness*. Two years prior to admission the patient had noted the sudden onset of erythema and edema of the eyelids and neck. Shortly thereafter she noted edema of the hands and complained of mild chills and

*Autopsy and general pathological examination performed by Dr. F. Jennings.

low-grade fever. Topical therapy and systemic antibiotics produced no improvement. Eight months PTA, following onset of a generalized weakness with the appearance of new skin lesions over the shoulders and arms, the patient was hospitalized at another institution. A skin and muscle biopsy confirmed the clinical impression of dermatomyositis and the patient was treated for several months with cortisone, ACTH, and testosterone.

Fig. 4—Photograph of the mucosal surface of a section of duodenum just distal to the pylorus. Numerous mucosal ulcerations can be seen.

In October, 1954, she had a further exacerbation of chills, fever, dermatitis, and muscular weakness and was seen for the first time in the Dermatology OPD of the AMBH. Following a diagnosis of dermatomyositis adrenal steroid therapy was gradually discontinued while testosterone injections were given twice weekly. In November, 1954, she was hospitalized at the AMBH for biopsy of a mass in the right breast which histologically showed fat necrosis. With

renewed progression of her dermatitis and generalized weakness she was hospitalized at the AMBH for the second time on January 5, 1955.

On physical examination the vital signs were normal. An erythematous, telangiectatic, scaling eruption was seen over the face, neck, shoulders, arms, abdomen, and thighs. There was severe edema of the hands. The scalp showed diffuse alopecia. The surgical incision in the right breast had not healed. Except for hoarseness the patient showed no other abnormalities.

Significant laboratory data included Hgb. 8.5 gm. and R.B.C. 3.27 million; W.B.C. 6,700 with 86 per cent polys, 12 per cent lymphocytes, and 1 per cent eosinophiles; total protein 8.0 gm. per cent with albumin 3.5 mg. per cent and globulin 4.5 gm. per cent; persistently 4 plus guaiac stools, many of which were grossly bloody; and urinary creatine of 0.38 gm. and urinary creatinine of 0.64 gm. in 24 hours. On proctoscopy the rectal mucosa was friable and showed several well circumscribed ulcerations. X-ray examinations of the upper gastrointestinal tract and the large bowel revealed no abnormalities.

The patient was treated with testosterone injections and blood transfusions but her course was steadily downhill. Six days prior to death she developed a bloody diarrhea and two days later she was started on ACTH therapy. On the 33rd hospital day the patient developed persistent vomiting of bile-stained fluid and expired six hours later.

Gastrointestinal examination:—The distal half of the esophagus showed several deep penetrating ulcers, the largest measuring 10 x 6 mm. and extending almost through the muscularis (Fig. 3). A cluster of irregular confluent ulcers was seen at the cardia.

The stomach contained 1,000 c.c. of bile-stained fluid. The mucosa was smooth. There was moderate submucosal congestion at the fundus. In the antrum there were several ulcerations measuring up to 1 cm. in diameter and extending into the muscularis.

The mucosa of the first portion of the duodenum revealed a small number of ulcerations similar to those observed in the antrum (Fig. 5). The 2nd and 3rd portions of the duodenum were dilated with a circumference measuring 12 cm. Following an abrupt transition the circumference of the 4th portion of the duodenum measured 6 cm. Passing across the superior surface of the duodenum at the junction of the 3rd and 4th portions was a small branch of the superior mesenteric artery which compressed the duodenum but did not produce total occlusion. The main branch of the superior mesenteric artery was normal and normally situated.

Except for 3 small polyps the jejunum was normal.

The terminal ileum showed a flattened mucosa and a few small mucosal ulcerations.

There was considerable hyperplasia of the mucosal pattern throughout the colon, with many small mucosal tufts appearing as incipient polyps. The wall of the entire colon was thickened. The rectal mucosa was congested and hyperemic. The mucosa was intact throughout the large bowel.

Histopathological examination:—The esophagus showed intense peptic esophagitis with a polymorphonuclear infiltrate extending through the muscularis. Much of the mucosa was missing and there was marked submucosal edema.

Numerous ulcerations were present in the stomach and these penetrated deeply into the submucosa, in some areas forming submucosal abscesses. The muscularis showed inflammatory changes.

Sections from the duodenum showed changes consistent with early infarction. The jejunum showed submucosal hemorrhage and some of the submucosal

Fig. 5—Case 4. Photograph showing generalized denudation of epidermis which had been preceded by a bullous eruption of the skin.

vessels showed intimal proliferation. Infarction was seen at the base of a jejunal polyp.

There was focal submucosal thickening and hemorrhage with considerable edema in the colon. Focal hemorrhagic areas of mucosal epithelium gave the appearance of infarcted incipient polyps. In these areas there was also marked round cell infiltration in the mucosa.

Case 4:—Mrs. E. T., a 62-year old Negro housewife, entered the AMBH on January 8, 1955, complaining of generalized muscular weakness and dysphagia of six weeks duration*. Her symptoms first began with weakness of the legs and shortly thereafter she noted dysphagia coincidentally with the appearance

*Autopsy and general pathological examination were performed by Dr. E. Humphreys, Dr. M. Lavia and Dr. G. Martin.

of a dermatitis over the face, chest, and extensor surfaces of the extremities. Two weeks PTA weakness developed in both arms and this was of such severity that the patient was unable to feed herself. Following further generalized impairment of muscular strength, the patient was hospitalized.

Physical examination revealed a well-developed female with evidence of recent weight loss and markedly impaired muscular strength. An erythematous, telangiectatic, scaling dermatitis was present over the eyelids, nose and cheeks, upper chest, and extensor surfaces of the upper extremities. There was pronounced weakness of the proximal muscle groups of all extremities with lesser weakness of the distal muscle groups and musculature of the trunk. The patient was unable to sit unassisted from a supine position, raise her hands to her mouth, or turn over in bed without assistance. There were muscle contractures of both elbows and the proximal joints of the 2nd and 3rd digits of both hands. No other notable findings were observed on examination.

Significant laboratory data were as follows: R.B.C. 4.85 million on admission with Hgb. 13.0 gm., the Hgb. falling to 7.9 gm. just prior to death; W.B.C. 10,650 with normal differential count; total protein 5.8 gm. per cent with normal A/G ratio on admission and 3.2 gm. per cent albumin and 3.4 gm. per cent globulin 1 month later; urinary creatine 0.67 gm. and urinary creatinine 0.60 gm. in a 24-hour specimen. Skin and muscle biopsies were compatible with dermatomyositis. Repeated stool examinations for blood were negative. On x-ray examination with barium the esophagus showed delayed transit time with impaired peristalsis; normal mucosal folds were not visualized after passage of the barium. A small diverticulum was seen in the lower esophagus. Further x-ray examinations with barium revealed no abnormalities in the stomach, small bowel, or large intestine.

Following a diagnosis of dermatomyositis the patient received testosterone propionate injections twice weekly together with general supportive therapy. At the end of the first month of hospitalization, during which there was little change in her condition, she developed pneumonitis and was treated with intramuscular penicillin. Shortly thereafter muscular weakness showed further progression and the patient's caloric intake rapidly diminished. Testosterone was discontinued and large doses of ACTH were begun. Two weeks later the patient developed a generalized bullous eruption with denudation of large areas of the skin surface. Thereafter her condition rapidly deteriorated despite blood transfusions, tube feedings, and continued adrenal steroid therapy, and she expired ten days later.

Gastrointestinal examination:—The esophagus showed a severe peptic esophagitis.

There was marked atrophic gastritis of the stomach with numerous large areas of hemorrhagic necrosis. The rugal folds were entirely lost.

The small intestine was normal.

Except for multiple diverticula in the colon no abnormalities were noted.

Histopathological examination:—The mucosa of the distal half of the esophagus showed many areas of necrosis and absence of epithelium. There was dense fibrosis and some small cell inflammatory infiltrate throughout the submucosa. All muscle layers showed marked focal atrophy with replacement by dense connective tissue in affected areas. The small arteries appeared to be increased in number and thickening of the walls with hyalinization of the muscular layer was observed in many vessels. Luminal obliteration and throm-

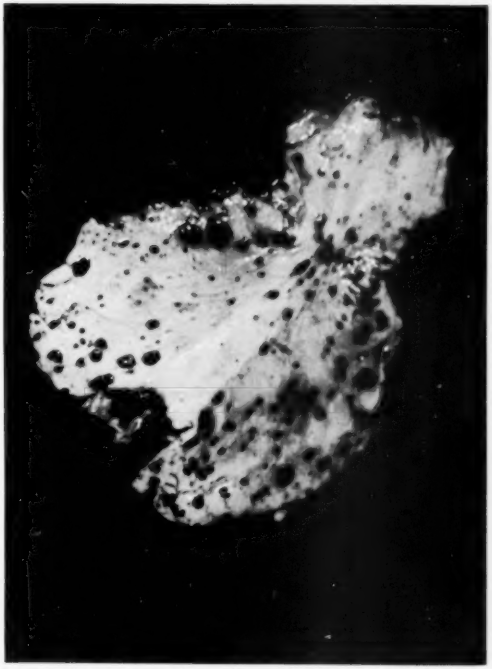

Fig. 6—Case 4. Photograph of mucosal surface of the stomach showing numerous sharply circumscribed areas of hemorrhagic necrosis.

bosis of some affected arteries were seen. Marked varices were noted in the venous system.

There was considerable fibrosis about many of the myenteric plexi and in some instances degenerative changes in nerve fibers were apparent. There seemed to be some reduction in the number of plexi observed. Similar changes in these same structures were noted in sections from the stomach, small intestine and large bowel.

The stomach showed some necrosis of the mucosal epithelium. Little change was observed in the muscular layers. The small arteries again appeared

to be increased in number and there was some thickening of blood vessel walls although the vascular changes were not as severe as those seen in the esophagus.

Both the small intestine and large bowel showed areas of microscopic ulceration. Changes in the walls of the small arteries were similar to those noted in the stomach. Some sections showed marked thickening and hyaline changes in the blood vessel walls associated with luminal obliteration and recent thrombosis.

Lupus Erythematodes

Symptoms referable to the gastrointestinal tract are commonly encountered in acute systemic *lupus erythematodes*. In a recent survey of 62 cases Dubois[25] noted that gastrointestinal disturbances comprised the presenting symptoms in 10 per cent of cases and that 40 per cent of the patients had such complaints during some stage of their illness. When present the symptoms are similar to those seen in other diffuse connective tissue diseases: anorexia, dysphagia, nausea, vomiting, diarrhea, and constant or cramping abdominal pain. Tarry or grossly bloody stools are occasionally found. In rare instances acute onset of abdominal pain associated with rebound tenderness may progress to simulate an acute surgical abdomen. Paralytic ileus complicating systemic *lupus erythematodes* has also been described[26].

Postmortem examination often reveals peritonitis, and Reifenstein et al[27] reported this finding in 72 per cent of their cases. It is the peritoneal serositis which is held to be responsible for the symptomatic complaint of abdominal pain. Mesenteric edema, petechiae and diffuse hemorrhage of the bowel wall may also be seen at necropsy[25]. In the series of 138 patients recently reported by Harvey et al[26] 7 had esophageal lesions on autopsy examination: 4 of these showed mucosal ulcerations and 3 showed diphtheritic esophagitis. These authors describe seven additional patients with intestinal ulcerations, 3 showing lesions in the small intestine and 4 in the large bowel.

Histologic examination of the intestinal wall[26,28] may reveal marked edema and fibrinoid degeneration of the connective tissue with a small cell inflammatory infiltrate. Fibrinoid changes in the connective tissue of the vessel walls are not uncommon and resultant infarction and hemorrhage may occur. Such blood vessel changes are usually seen at the bases of the intestinal ulcerations, although they may occur diffusely throughout the bowel in the absence of such lesions[28].

Case 5:—Miss G. G., a 13-year old white girl, was first admitted to Bobs Roberts Memorial Hospital of the University of Chicago Clinics in February, 1950, because of arthralgias and low grade fever*†. Her illness had begun 13

*Autopsy and general pathological examination by Dr. E. Humphreys, Dr. J. Green and Dr. G. Martin.

†Permission to publish this case was granted by Dr. A. Dorfman.

months prior to admission with a "butterfly" erythema over the nose and malar eminences, and this was followed 4 months later by an episode of right lower quadrant pain, nausea, vomiting, and low-grade fever. The gastrointestinal symptoms shortly subsided but they were immediately followed by progressive easy fatiguability, anorexia, intermittent fever to 103°, and pain and swelling in the small joints of the fingers bilaterally. With persistence of these symptoms the patient was hospitalized for further evaluation and treatment.

Physical examination revealed a moderately well-developed, well-nourished female who appeared chronically but not acutely ill. Except for a pulse rate of 100 the vital signs were normal. There was a marked erythema over the malar eminences and cheeks and similar changes were observed over the skin of the buttocks. There was striking nontender adenopathy in the submental, anterior and posterior cervical, axillary, epitrochlear, and inguinal regions bilaterally. The remainder of the physical examination was not remarkable.

Significant laboratory data included Hgb. 11 gm. with HMCT 39 per cent; W.B.C. 3,100 with normal differential, and sedimentation rate 35 mm./hr. Urine examination was normal except for occasional RBC's in the urinary sediment; PSP excretion was 80 per cent in 1 hour. Skin biopsy showed changes consistent with *lupus erythematodes.*

Following a diagnosis of acute systemic *lupus erythematodes* treatment was begun with ACTH. After moderate control of her symptoms the patient was discharged from the hospital.

In the following 3½ years she was readmitted to the hospital on 13 occasions, usually because of recurrent specific skin lesions and acute onset of gastrointestinal symptoms of nausea, vomiting, and diarrhea. On one occasion dysphagia and melena were prominent complaints. Throughout this period she was given numerous courses of ACTH therapy which produced only partial remissions. In July, 1953, the patient suddenly began having convulsive seizures. Three months later there was abrupt onset of diplopia associated with severe memory loss, and the patient was hospitalized for the last time in October, 1953.

Upon admission she was found to have a septicemia due to hemolytic staphylococcus aureus. Despite treatment with massive doses of penicillin her condition rapidly deteriorated. On the 5th hospital day she became comatose and shortly thereafter expired.

Gastrointestinal examination:—The esophagus, stomach, small intestine, and colon up to the sigmoid showed no remarkable changes.

In the mucosa of the sigmoid and rectum there were several ulcerations which appeared to be acute, the largest in the sigmoid measuring 1.3 cm. in diameter. There was no induration about the margins of these ulcers.

Histopathological examination:—The esophagus showed focal superficial erosions of the mucosa with chronic inflammatory cell infiltration in the *lamina propia*. There was some thickening and fibrosis of the submucosa.

Sections from the stomach and ileum showed no unusual changes.

In the rectum there was subacute ulceration and some perivascular, principally mononuclear, inflammatory cell infiltration around the ulcer bed. The submucosa showed moderate fibrosis. Edema and inflammatory changes were noted in the muscle layers. The muscle was hypertrophied but there was some replacement of muscle fibers by dense connective tissue near the ulcer bed. Adjacent to the ulcer was a thrombosed submucosal vessel, and there was degenerative swelling in the wall of an adventitial artery well below the ulcer floor. In the fat just outside the bowel wall intimal edema and degeneration were noted in the wall of a vein.

In another section a more acute rectal ulcer was seen with fresh necrotic changes. Acute fibrin vascular thrombi and hemorrhage were observed in the underlying submucosa. To one side of the ulcer there were thromboses in the capillaries of lymph follicles.

Summary

The symptoms, clinical findings, and pathological alterations that may occur in the gastrointestinal tract as a manifestation of diffuse connective tissue disease have been discussed with reference to scleroderma, dermatomyositis, and acute systemic *lupus erythematodes*.

Pertinent case material has been presented.

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Discussion

Dr. I. Snapper:—Dr. Rothman has clearly demonstrated how important scleroderma of the esophagus is for the gastroenterologist. The rest of the intestine is also involved in scleroderma but less frequently. If the epithelium of the small intestine is involved, a sprue-like syndrome may ensue. I have been able to observe a case of typical osteomalacia, following fatty diarrhea due to scleroderma. This woman was carried in on her husband's arms because multiple pathologic fractures prevented her from walking. After treatment with ultraviolet light the skeleton completely healed but the scleroderma was progressive. I saw her a few days ago with typical multiple sclerodermatous ulcers of the legs.

In a patient with scleroderma and difficulty in swallowing, we should only diagnose scleroderma of the esophagus if the typical x-ray findings which Dr. Rothman described are present, that is a wide esophagus with a narrowing near the cardia. If there is apparent scleroderma of the skin, difficulty in swallowing, but without widening of the esophagus and, especially without narrowing of the cardia, then another disease, i.e. primary amyloid of skin and esophagus, is present. In primary amyloid of the esophagus, there is often also widespread amyloid of the deep layers of the corium. As a reaction to the amyloid degeneration of the subcutaneous area, the epidermis changes and the clinical and microscopical picture of scleroderma ensues.

Thus in primary amyloid a pseudoscleroderma of the skin, with difficulty in swallowing may be present. In such cases, however, the esophagus is not dilated and there is no narrowing of the esophagus above the diaphragm.

Another very frequent sign of scleroderma of the gastrointestinal tract is widening of the third portion of the duodenum. Nearly every patient with scleroderma of the esophagus presents this anomaly of the duodenum.

As Dr. Rothman has so well explained, the corticosteroids work best in *lupus erythematosus*, sometimes in dermatomyositis, and relatively rarely in scleroderma. If anything, the danger of corticosteroid treatment is especially apparent in scleroderma because scleroderma, as Dr. Rothman has emphasized, is no skin disease. It is a very widespread disease, and many different organs may be involved. The sclerodermatous changes of the smaller renal arteries, and of the periarterial tissue explain why, in patients with scleroderma, much more than in other patients, during treatment with corticosteroids, high blood pressure with acute left heart failure readily develops. Some scleroderma patients who are treated with corticosteroids may only present slight headache and a moderate hypertension in the afternoon but may suddenly die during the night of left heart failure.

I am glad Dr. Rothman does not accept that *lupus erythematosus*, *periarteritis nodosa*, and dermatomyositis are identical. Many clinicians have been guilty of identifying these three diseases as allergic manifestations. These diseases can easily be differentiated by their clinical characteristics. In addition the reaction of these diseases on corticosteroid treatment is not the same and the discovery of the lupus cell distinguishes *lupus erythematosus* from the other diseases.

Very interesting for us are the cases of dermatomyositis with intestinal and stomach lesions which Dr. Rothman has shown. When in ulcerative colitis the epidermis is rubbed off easily and vesicle formation is widespread, dermatomyositis must be suspected, even if there is no clinical involvement of the musculature. Most of these cases have a fatal course.

THE INDICATIONS FOR COLOSTOMY*

MANUEL E. LICHTENSTEIN, M.D.†

Chicago, Ill.

Colostomy is an artificial opening in the large bowel which permits the passage of fecal matter and gas in whole or in part elsewhere than through the normal channel or anus. The opening may be external onto the abdominal wall or internal into a more distal segment of bowel. A colostomy is necessary for the following purposes:

1. To decompress distended large bowel due to obstruction.
2. To divert the fecal current from the distal colon:
   a) in preparation for resection of an obstructive lesion.
   b) to permit extensive surgery about the rectum, anus or perineum in selected cases.
   c) to permit healing of injuries and to favor resolution of an inflammatory process in the distal colon.
   d) when an irremovable lesion becomes obstructive.
3. To allow for resection of a segment of colon that is the seat of inflammatory or neoplastic disease, volvulus, gangrene or severe injury when primary closure is impossible or undesirable.
4. To serve as an artificial anus when the distal segment of the colon is removed.

The variety in types of colostomies makes it possible to apply to each patient that type which will serve the most useful purpose. The following classification and description of colostomies is presented with the hope that selection of the type most appropriate for the indication will give relief to the patient with a minimum of inconvenience and without unnecessary risk:

Types of Colostomies

I Colostomy in continuity (Fig. 1)

1. External decompression (cecostomy)

a. active, b. passive

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†Associate Professor of Surgery, Northwestern University Medical School. Professor of Surgery, Cook County Graduate School of Medicine.

2. Internal decompression (ileocolostomy and colocolostomy)

a. active, b. passive

II Colostomy in discontinuity (Fig. 2)

1. External 2. Internal

III Colostomy with a spur (Fig. 3)

1. With bowel resection (obstructive resection)—
(double-barreled colostomy)

2. Without bowel resection ("temporary" colostomy)

IV Colostomy on end (Fig. 4) (artificial anus)

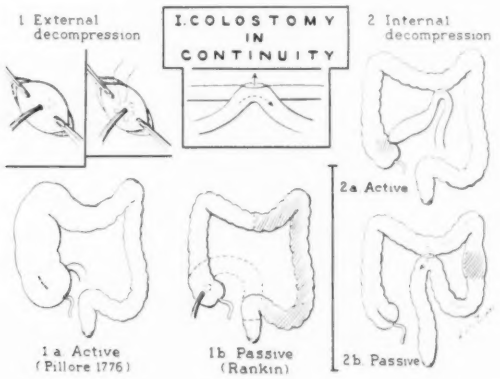

Fig. 1—Colostomy in continuity. A vent to permit decompression of distended bowel or to prevent distention in normal bowel.

Colostomy in Continuity

This operation is done to decompress the large bowel with no design for complete diversion of the fecal current.

1. External decompression, a) active:—This type of colostomy is best illustrated by the cecostomy made to relieve acute large bowel distention with impending perforation at the cecum. When the abdomen is markedly distended, a scout film of the abdomen shows tremendous dilatation of the cecum, and no relief from distention is obtained either by the use of enemas, by attempted intubation of a low lying lesion, or by the knee-chest position to effect reduction of a lesion intussuscepted into the distal colon, cecostomy will decompress the bowel with the least risk to the patient. This will avoid perforation, restore the circulation of the bowel to normal, diminish the virulence of the intestinal

flora, reduce edema, promote healing at the site of ulceration and obstruction, and make possible the preparation of the patient for surgery pertinent to the lesion responsible for the obstruction. Cecostomy will fail as a decompressive procedure when the bowel is not exteriorized and the opening is too small to permit a free exit of its contents. Retraction of the stoma is always a hazard due to failure to *mobilize and exteriorize the cecum.* The wound in the abdominal wall should not be tightly closed as this favors infection, sepsis, sloughing of tissue and herniation. The application of dry dressings helps to avoid anaerobic infection. Cecostomy is not intended for complete diversion of the fecal current.

1. External decompression, b) passive:—In the course of surgery on the colon it is sometimes noted that an end-to-end anastomosis is made in bowel that is not fully decompressed or completely free from edema. While there

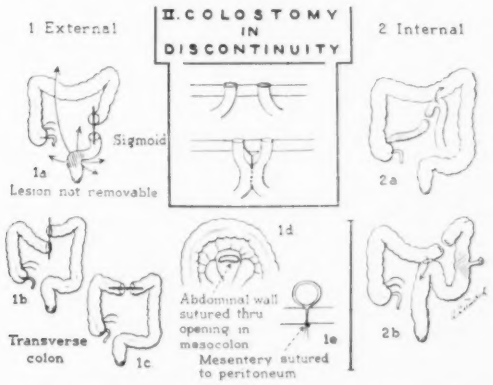

Fig. 2—Colostomy in discontinuity. Complete separation of the proximal and distal stomata. Actual diversion of the fecal current is accomplished.

may be good reason for rejecting the operation under these circumstances, it is not always necessary to do so, for a tube placed in the cecum for large bowel decompression may prevent further distention and permit complete subsidence of the local disturbance. This prophylactic decompression by means of a tube in the cecum was of frequent use in the past but is practiced infrequently at present. Newer methods of bowel preparation before surgery is done and more detailed postoperative management have made this procedure relatively unnecessary. When indicated, however, it is a safety factor which may prevent a catastrophe. It, therefore, should not be discarded as obsolete but kept on call in the surgical repertoire. *Exteriorization of the cecum for this type is not necessary.* The insertion of a large "mushroom" catheter into the cecum is adequate to maintain decompression when obstruction is no longer present.

2. Internal decompression, a) active:—This type of colostomy (ileocolostomy (or colocolostomy) does not completely sidetrack the fecal current but it does decompress distended bowel proximal to the site of obstruction and permits the passage of most of the fecal matter into the distal colon. It is useful in inflammatory and irremovable malignant lesions that involve the cecum or the colon. Frequently this procedure permits complete healing of ulcerative or inflammatory disease and also makes possible resection of tumors following subsidence of a complicating inflammatory process.

2. Internal decompression, b) passive:—In some instances an internal colostomy is desirable to avoid an impending obstruction or to permit healing in an inflamed segment of bowel which is not obstructed. Chronic granuloma, ileitis, or an irremovable malignant lesion may be sidetracked to permit healing or prevent obstruction.

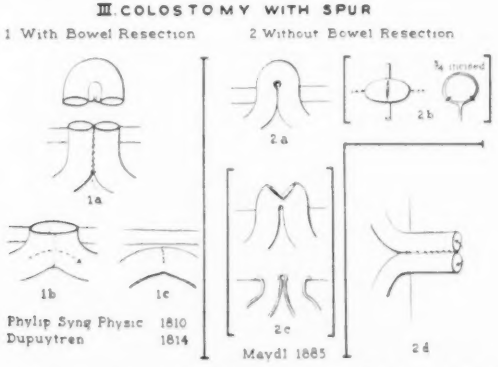

Fig. 3—Colostomy with spur. 1. With bowel resection—double-barreled colostomy following obstructive resection. 2. Without bowel resection for decompression and diversion of the fecal current.

Colostomy in Discontinuity

The purpose for which this operation is done is complete diversion of the fecal stream with defunctionalization of the distal colon. Actual separation of the proximal and distal lumens makes this a certainty.

1. External:—Figure 2—1a to 1d. This type of colostomy is commonly made in the sigmoid colon as a palliative procedure when exploration of the pelvis discloses widespread malignant disease arising in the rectum, precluding any possibility of excision. Colostomy in discontinuity will relieve the patient of the distress caused by contamination of the ulcerated lesion by fecal matter, diminish the loss of blood from the infected lesion, prevent the total bowel obstruction which is usually inevitable in such instances, and avoid the serious urinary complications when the colonic lesion perforates into the bladder. It

may be properly done following decompression of a markedly distended bowel by cecostomy or on a patient prepared for exploration of the abdomen. It should not be done on the senile patient, the mentally depressed, or the patient who is not obstructed on a nonresidue diet.

This type of colostomy is frequently necessary for extensive injuries to the rectum and for inflammatory disease (diverticulitis). It is made on the right side of the abdomen in the transverse colon. Thus the left side of the abdomen is free from an operative wound and permits definitive surgery later

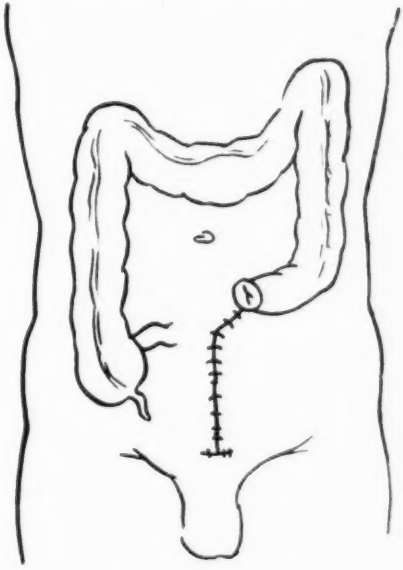

Fig. 4—Colostomy-on-end. Terminal colostomy. Artificial anus.

in the left colon with less difficulty. Unlike colostomy in continuity, sufficient bowel and mesentery are required to exteriorize the entire segment without tension. Complete separation of the proximal and distal stomas is the basis for its usefulness.

2. *Internal:*—Under certain circumstances, as when an inflammatory mass in a segment of bowel is followed by an external fistula, a sidetracking operation may permit healing of the lesion. Drainage from the fistula may persist, however, as long as fecal matter passes into the involved segment of bowel. Under these circumstances closure of the bowel between the anastomosis and

the lesion allows complete healing to take place. Thus, complete diversion of the fecal stream is accomplished.

Colostomy with a Spur

1. With bowel resection:—This type of colostomy is usually but not always constructed as incidental to resection of an exteriorized segment of bowel. It is useful in volvulus, extensive trauma, inflammatory disease such as diverticulitis, bowel strangulation, and in some instances of carcinoma. The proximal and distal limbs of the exteriorized bowel are approximated by one or two rows of sutures placed on the antimesenteric border of the bowel; the involved segment is removed; and a double-barreled colostomy is established. The operation is often called "obstructive resection" and is preferable to primary anastomosis under the following circumstances:

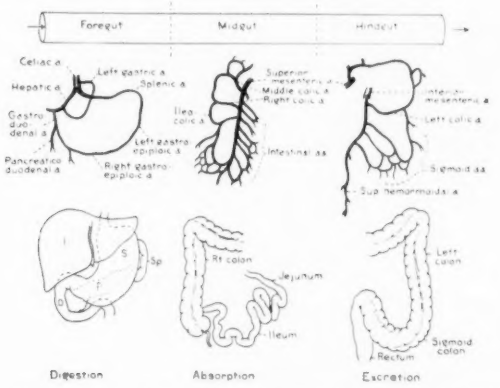

Fig. 5—The right colon is part of the absorptive portion of the gastrointestinal tract. Its content is liquid. Openings here give a "wet colostomy". The left colon is the excretory portion of the gastrointestinal canal. Openings here give a "dry" colostomy.

a. When great disproportion is present in the size of the lumen of the bowel proximal and distal to the lesion accompanying subacute or chronic obstruction.

b. When pericolonic infection or abscess is a contraindication to primary resection.

c. In the presence of an excessively fat mesentery obscuring the vascular pattern or an extensive, contaminated raw surface devoid of peritoneum.

d. In the absence of well-prepared bowel in an elderly patient with concomitant disabilities.

e. Where free perforation with spreading peritonitis occurs and the lesion requiring resection can be mobilized and exteriorized from the abdomen.

Following resection of the lesion and the removal of all clamps, the spur which separates the two lumens is crushed and allowed to slough, or it may be double clamped, incised between clamps and each side sutured so that continuity of lumens is restored. This type of colostomy is thus converted into a colostomy in continuity and may be closed as soon as circumstances allow.

2. *Without resection:*—(Fig. 3–2a) In this type a loop of colon is brought up through an opening in the abdominal wall and suspended on a rod or tube placed through an opening in the mesentery between the bowel and the marginal artery. It is more readily done in the transverse or sigmoid segments of the colon. It may be done on fixed segments of bowel only following adequate mobilization. This requires manipulation and is not easily accomplished when marked distention of the bowel is present. An inadequately mobilized segment of bowel under tension on the abdominal wall will slough

Fig. 6—Perforation of the cecum in left colon obstruction.

at the site of suspension over a rod and defeat the purpose for which this procedure is done. It is the least troublesome of all colostomies to establish and is therefore more commonly made. It is indicated in large bowel obstruction when distention has not progressed to such an extent that manipulation would encourage perforation at the cecum. Colostomy with a spur is used also to sidetrack the fecal stream from bowel that is the site of diverticulitis with or without fistula formation. It does not always do so as efficiently as the colostomy in discontinuity.

In some instances exteriorization of a freely movable segment of normal transverse or sigmoid colon is done and approximation of the proximal and distal limbs effected as shown in Figure 3–2d. The protruding bowel is now sectioned at its apex, and diversion of the fecal stream is accomplished. Long limbs of protruding bowel aid in diverting the fecal stream as in colostomy

in discontinuity. This has been used for injuries to the rectum. Following healing in the pelvis, closure of the double-barreled colostomy is effected by crushing the spur and closing the stoma. Thus, the colostomy with a spur is a type convertible from one of discontinuity to one of continuity.

Colostomy on End

This type is the artificial anus that remains following complete excision of the distal colon, rectum, and anus. The stoma is placed according to the practice of the surgeon and the available segment of bowel at a convenient place on the abdominal wall preferably through a separate opening and not through the primary surgical wound.

A colostomy in the right colon requires considerably more care and attention because of the liquid fecal matter here than one in the left colon where the fecal matter is formed (Fig. 5).

Cecostomy Versus Transverse Colon Colostomy

An obstructed and markedly distended large bowel must be decompressed lest perforation occur at the cecum or at the site of the obstructing lesion. Two procedures have been suggested, cecostomy and transverse colon colostomy. The choice between the two is dependent upon several factors.

The transverse colon colostomy when properly done not only permits decompression of the large bowel but also to some extent aids in sidetracking the fecal current. It is indicated in large bowel obstruction with moderate distention especially when the obstructing lesion is located low in the sigmoid or rectum. It may be combined with a limited exploration to determine the exact site of the lesion, the extent of lymph node involvement, and the presence of metastases. Exploration, however, is not without danger in large bowel obstruction with marked distention. The objections to transverse colon colostomy are: 1. When bowel is markedly distended, manipulations incidental to liberating and exteriorizing the colon may result in perforation of the cecum. The latter may occur in spite of a transverse colon colostomy. Constriction of the proximal limb may relieve distention in the distal colon and still maintain distention at the cecum. Torsion of the loop may do the same. If mobilization of the colon is inadequate, especially when the omentum and the gastrocolic ligament are not divided, the transverse colon colostomy may retract and serve only as a colostomy in continuity. 2. The most serious objection to the universal use of the transverse colon colostomy is that in obstructive lesions that involve the left colon above the rectosigmoid the definitive operation for removal of the obstructive lesion in the bowel and its mesentery with contained lymph nodes may require an anastomosis between the right transverse colon and the rectum. The presence of a colostomy in the transverse colon will make such

an operation time-consuming, difficult if not impossible, and hazardous. Thus the transverse colon colostomy may defeat the objective of wide resection.

Cecostomy permits exposure of the most vulnerable portion of the large bowel, the site that most commonly perforates in complete large bowel obstruction (Fig. 6). It has been found repeatedly that satisfactory decompression of the large bowel usually gives relief from edema at the site of the obstructing lesion and permits bowel movements to occur through the normal passage. When properly constructed it permits irrigation of the distal colon, and with the administration of cleansing enemas the entire bowel may be completely emptied. It is particularly useful when the lesion in the left colon is above the level of the sigmoid. A wide resection of bowel and mesentery will permit the use of a free transverse colon which may be anastomosed to the lower sigmoid or rectum.

Objections to cecostomy are due to two misconceptions. First, the objection that it does not sidetrack the fecal current is not valid since this procedure was never designed to do so. When marked distention occurs and the risk of perforation is great, decompression is urgent. Cecostomy will do this no matter where in the large bowel the obstructing lesion is located. Volvulus must of course be excluded, for neither the cecostomy nor the transverse colon colostomy will relieve the distended loop in the sigmoid. The second objection is that it does not empty the bowel readily nor effectively. This occurs only when a small tube is inserted in the ceum. Exteriorization of the cecum with formation of a large opening facilitates a more prompt decompression and also permits irrigation of the bowel. One must appreciate that the large bowel is not a rubber balloon. An opening made in the cecum does not cause immediate collapse of the distended bowel. Smooth muscle fibers that have become elongated require time to regain tonus at a shorter length and it may take several days before the contained fecal matter is emptied through the cecal opening. After several days irrigations may be instituted to dilute the fecal matter and facilitate its removal. Enemas may now be commenced from below, and by the end of a week most of the distention will have receded. With the patient on a nonresidue diet further filling with fecal matter is avoided. Even a transverse colon colostomy will require irrigations to empty the distal segment.

The patient who has not been completely studied because of the seriousness of his illness and the emergency nature of the cecostomy may, during the days required for decompression, have a more thorough study undertaken and restorative measures instituted for rehabilitation. Elderly patients who require a decompressive operation on the large bowel usually are in poor condition with cardiac and pulmonary complications, anemia, uremia, sepsis or other disabilities usually responsible for a high mortality rate. These conditions may be corrected during the time the bowel is decompressed and prepared for resection of the lesion responsible for obstruction.

Summary

The clinical indications for colostomy have been stated. Tumors, inflammatory disease, trauma and anatomical defects involving the colon, rectum and anus present the circumstances for which colostomy is required. In each, the type of colostomy to be made varies with the nature of the disease and the complications present at the time the patient is first examined.

Carcinoma

It is unfortunate that many colostomies are made because of carcinoma in the colon. Most of them could be avoided if victims of malignant or potentially malignant lesions were examined and cared for soon enough.

The use of the anorectosigmoidoscope and competent x-ray studies of the colon to demonstrate the mucosal pattern before symptoms or physical signs are noted will visualize small early lesions and permit surgical care appropriate to the location and character of the lesion. Thus, decompressive, sidetracking and palliative colostomies would become unnecessary. Carcinoma uncomplicated is asymptomatic and must be sought out for early recognition.

Acute and Chronic Inflammatory Lesions

Primary resection during the acute process is not always possible. Exteriorization of the involved segment of bowel with formation of a double-barreled colostomy is possible when the lesion can be mobilized adequately.

In many instances a transverse colon colostomy is necessary to decompress the bowel and sidetrack the fecal current before resection of the involved segment of bowel can be done. Following this the colostomy may be closed. Volvulus, gangrene and traumatized bowel under circumstances unsuitable for resection and primary closure are handled in a similar manner.

Wounds in the Extraperitoneal Rectum and Perineum

Diversion of the fecal current by avoiding fecal contamination permits healing of wounds. This is especially useful when surgical repair of the injury is impractical. Even when repair of extensive wounds can be done, the avoidance of fecal contamination by diversion is a useful procedure.

COLECTOMY DURING ACUTE PHASE OF CHRONIC ULCERATIVE COLITIS*

MORRISON SCHROEDER, M.D.

Milwaukee, Wisc.

Ulcerative colitis is usually thought of as a chronic disease with a tendency to frequent exacerbations of varying severity. Some have regarded it as incurable[6]. Although it is probably a systemic disease of unknown cause, its most important manifestations are referable to the colon, and much of the therapy is directed to the colon. Many patients with ulcerative colitis get along for years with proper medical therapy. In the experience of the Veterans Hospital, Wood, Wisc., however, 46 per cent of those hospitalized with the disease have come to operation. In the cases that do not improve or that deteriorate in spite of proper vigorous medical measures, surgical treatment may become necessary. The following report is of such a case:

A 21-year old, white, female secretary was admitted to the hospital on January 8, 1954. Except for a poor appetite and occasional episodes of diarrhea, she had been well until two months before admission. At that time, she began to have about two loose bowel movements daily and her appetite became worse. A month before admission, diarrhea had increased to five times daily. Two weeks before admission, there was blood in the stools. At that time, proctoscopy revealed small ulcerations in the rectum, and barium enema was consistent with the diagnosis of ulcerative colitis. At the time of admission, the patient appeared ill and pale. The abdomen was soft and not tender. Temperature 103°, pulse 130, hemoglobin 10.5 gm., WBC 8,000 with 65 per cent polys, sedimentation rate 47, total serum protein 5, albumin 2.5, prothrombin 52 per cent. She was put on a bland, low residue diet, given vitamins, belladonna, and sulfasuxidine. Fever, however, to 102 and 103° daily, persisted. She deteriorated in the hospital, became nauseated, vomited, and became lethargic. The abdomen became somewhat distended and moderately tender. Anemia progressed, the hemoglobin being 8.2 gm. the third day after admission. She was given blood and plasma. Because of nausea, the problem of nutrition became acute. On January 17, the ninth day after admission, she was vomiting, there was more abdominal pain, and the abdomen was somewhat tense and tender. There were two massive, bloody bowel movements that day, and the hemoglobin had dropped from 12.8 to 10 gm. during the previous 24 hours. It was felt that the patient was losing ground rapidly and that colectomy was indicated.

Operation was undertaken as an emergency that same Sunday evening. There were about 500 c.c. of turbid, brownish yellow fluid in the peritoneal

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cavity. The large intestine was thickened and edematous, as was the distal 10 inches of ileum. The entire colon down to the midsigmoid and the distal ileum were removed. The ileum was brought out as an ileostomy to the right of the umbilicus. The sigmoid segment was brought out as a fistula through the caudad extremity of the wound. During the procedure, the patient received 1,500 c.c. of blood (having had 1,000 c.c. of blood just prior to operation). The next day the patient looked less toxic. The temperature did not rise above 99.8°, having been 104° the day before. She continued to improve. A week after the operation, she was started on oral feedings. She was discharged from the hospital four weeks after the operation.

Although it is known that very occasionally there may be a dramatic, spontaneous subsidence of symptoms and fever in such a case of acute ulcerative colitis, in the past, such a problem would usually have been met by the performance of an ileostomy, the rationale being to divert the fecal stream and to allow the diseased colon to heal while it was at rest. Some patients have been saved by such treatment. The mortality of ileostomy alone in the acute cases, however, is quite high (57 per cent in our series—others have reported even higher rates) and the convalescence prolonged.

Death in acute fulminating ulcerative colitis may be due to peritonitis from perforation, hemorrhage, or toxemia. Inanition, malnutrition, embolus, and associated conditions such as cirrhosis, arthritis, and skin infections are additional factors that weigh against the patient's chances of survival. These conditions are not specifically dealt with by ileostomy. Therefore, after ileostomy, they may persist or grow progressively worse. Perforation, though uncommon, is an ever present danger. In cases of hemorrhage, bleeding may continue from the ulcerated colon. (In persistent or recurring hemorrhage elsewhere in the body, usually direct control of the bleeding is regarded as the best treatment, i.e. ligation of vessels in wounds, gastrectomy for bleeding ulcer, etc.) As much as 300 gm. of protein a day may be lost from the isolated colon[5]. In a patient whose nutritional status is already impaired and who is able to eat little because of nausea and lack of appetite, replacement of such loss is impossible. The colon remains as a source of infection and toxins may cause severe systemic disability. As Crile[2] has said, "These colons are in effect nothing more than a serosal sac filled with feces, pus, and blood, lined only with remnants of muscularis and mucosa. The physiologic effect of such a colon is comparable to that of an extensive third degree burn covered with a fecal poultice." Ileostomy itself introduces a problem of fluid and electrolyte control, and when these difficulties are added to those of blood, protein, and fluid loss from the diseased large intestine, the problem becomes more complicated. In our experience, ileostomy alone in the acute phase of ulcerative colitis is hazardous, the care of the patient very difficult, and the convalescence quite prolonged as compared with those patients having primary colectomy. The following case illustrates these points:

A 33-year old, white, single school teacher was admitted to a hospital on January 10, 1954. She had known that she had ulcerative colitis since 1947. Since that time there had been intermittent episodes of diarrhea. During the past year she had been somewhat worse, and during the previous six months she had complained of nausea, loose stools, and a weight loss of 12 pounds. A month before admission there had been blood in the stools. At the time of admission she was quite sick, her temperature being 103°. There was diffuse abdominal tenderness and some spasm. The hemoglobin was 7.5 gm. She was given various antibiotics and vitamins. She was placed on ACTH for two weeks. She was given a total of 47 units of plasma and whole blood. Bloody stools persisted, however, and her temperature varied between 102 and 104° daily. On February 19, 1954, 5 weeks after admission, a loop ileostomy was performed. Fever persisted, but gradually subsided. A portion of the ileostomy sloughed and an infection of the surrounding wound occurred. The patient gradually gained strength and the temperature subsided. Because the wound about the ileostomy could not be cared for properly, because of the long standing history, and the apparently irreversible disease of the colon, a colectomy was done on April 8, 1954, and the ileostomy was replaced. Subsequently, the patient did well, gained weight, and is now back teaching school.

It is interesting to compare these two patients. Their hospital admissions were within two days of each other and apparently each one was a victim of acute, severe ulcerative colitis with hemorrhage as a major problem. A review of the course of each patient, however, reveals the prompt subsidence of fever and the rapid improvement of the first patient following colectomy. Her total hospital stay was something over five weeks. Although the second patient survived and was ultimately rehabilitated, she was a very sick patient, necessitating numerous transfusions for a period of many weeks. Although the fever subsided somewhat after her ileostomy, her convalescence was prolonged and rapid progress did not result until after the colon had been removed. Her hospital stay totaled five months. It would seem that this patient might have been treated by primary colectomy with much more rapid rehabilitation, less risk, less morbidity, and much less expense.

Three patients had primary colectomy during the acute phase of ulcerative colitis in our hospital. One had a total colectomy with excision of the rectum at the same time. These patients did well after the operation, but one died three months postoperatively of hemorrhage from the splenic artery (splenectomy having been performed at the time of colectomy).

The indications for colectomy in acute ulcerative colitis are perforation of the colon, intractable hemorrhage, and failure to respond to adequate medical therapy. Although we have done resection of the rectum at the time of colectomy, it would probably be safer to leave the distal sigmoid and rectum when operating in the face of acute disease. These structures can be removed

at a later stage unless perforation and severe hemorrhage in them dictate their immediate removal[7]. Although primary ileorectal anastomosis at the time of colectomy for the acute disease has been described[1], few men of experience feel this procedure to be safe. We have never done it. Two patients have had reanastomosis of ileum and rectum some time after colectomy. One had to have the ileostomy reestablished one and one-half years after ileosigmoidostomy. The other was getting along fairly well, although proctoscopy one year after operation showed ulcerative colitis in the rectum which had not been involved at the time of colectomy.

The only point about technic to be mentioned here concerns the ileostomy. Much of the morbidity has to do with the ileostomy, obstruction, prolapse, maceration of the surrounding skin, and infection of the ileostomy wound. The frequency of the complications can be minimized by following suggestions of Dennis[4] (regarding the use of frozen section to eliminate involved ileum and regarding anchorage of ileum to the abdominal wall) and of Crile and Turnbull[3] (regarding the use of a mucosal graft to cover the protruding ileal segment). If it is impossible to suture the edge of the ileal mesentery to the right lateral abdominal wall, closure of the right gutter is done by suturing to the mesentery a flap of peritoneum from the lateral wall. The frequency of prolapse of the distal ileum and resultant obstruction makes this closure imperative.

Summary

In the acute phase of ulcerative colitis, when medical treatment has failed, primary colectomy with ileostomy can be done safely and with more rapid recovery of the patient than occurs after ileostomy alone. Colectomy prevents further loss of blood and protein, rids the body of a dangerous source of infection, and is indicated in perforation.

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Discussion

Dr. I. Snapper:—I want to congratulate Dr. Schroeder upon the results he obtained with the surgical treatment of ulcerative colitis. Nevertheless we must realize that patients with a permanent ileostomy, like the young lady from Milwaukee, are severely damaged people. A "cure" has certainly not been obtained. By definition these patients cannot have ulcerative colitis any more since they have no colon. But all the combined efforts of surgeons and psychiatrists together do not suffice to persuade us that such a young woman is a normal person.

There must be numerous occasions where she will sigh with the old philosophers: "Est vita, sed non est vita".*

Dr. Owen H. Wangensteen:—The hour is late, and I know you are all very tired. Unfortunately, we have not enough time, and neither your spirits nor mine are fresh enough to permit discussion of these important papers in the manner which their importance justifies.

In Utopias universal agreement is said to obtain on everything. In all the Utopias that I have read about, there seemed always to be an air of compulsion about that universality of agreement which was striven for. I believe a few honest expressions of differences of opinion are very desirable on controversial subjects.

I am familiar with the type of ulcerative colitis the authors described. It may be produced experimentally and may be observed following postganglionic sympathectomy; it may also be seen following the administration of large doses of mecholyl.

Were it not for the exceptional case in which long survival following conservative treatment occurs now and then in what looked like a hopeless situation—were it not for such occasional occurrences, I have the feeling that most of us would quite willingly capitulate to the idea that ulcerative colitis is not primarily a medical disease but a surgical disease.

In the last number of The American Journal of Gastroenterology [24:436-442, (Oct.), '55] you will find Dr. Karlson's interesting and informative paper of a year ago, in which Karlson and Dennis summarized the University of Minnesota experience with ulcerative colitis. The incidence of cancer in retained colons, in patients not undergoing colectomy for ulcerative colitis, and followed for a number of years, was 8 per cent. A similar experience is reported from the Massachusetts General Hospital; their figure for malignancy was about the same. I submit it is not good to treat any condition conservatively in which the expectation of malignancy is 8 per cent. Surgery can do better than that.

*Free translation: I live but is my life worthwhile.

In fact, I believe that if in an institution where this disease entity is being seen and treated, if the internists were willing, for a period of time, to send all their patients with acute ulcerative colitis to the surgeons, they would come out with more cured patients in a shorter period of time than by medical management alone.

We know from the Karlson-Dennis report that 50 per cent of patients treated medically for ulcerative colitis were dead. And 55 per cent of the patients reported by Warren and McKittrick, from the Massachusetts General Hospital, were dead. That is a big mortality. This large mortality was not at the hands of the surgeon but, occurred from a number of causes over a period of years. A mortality of 50 per cent within 10 years for ulcerative colitis treated medically should serve as a warning to suggest more energetic treatment.

In 1940 I did my first colectomy for acute fulminant ulcerative colitis such as Dr. Schroeder reported to us. During the intervening years, between then and 1948, I did several cases. Sometime later, my associate, Dr. Dennis, began to explore the role of vagotomy in ulcerative colitis and my contact with the problem came to a close. It is phenomenal, as Dr. Schroeder has pointed out, how one can excise the colon for a patient who is acutely ill with ulcerative colitis with hectic fever of the picket-fence type.

We shall never resolve this problem through recourse to dialectics. Will Mayo said long years ago, the bright day in medicine is always tomorrow, because only experience can prove the validity of a thesis. We must not argue on the basis of precedent as lawyers do. Facts count, not testimony.

I stood by long years ago and watched the son of one of my colleagues on our Faculty die from acute ulcerative colitis. As a last gesture, when distention occurred because of perforation and peritonitis, a decompressive colostomy was advised. How much better it would have been to have excised the colon. Now, with additional years of experience, we are able to save such patients by early colectomy in the manner described by Dr. Schroeder. Dr. Ripstein of Brooklyn has reported a unique experience with colectomy for fulminant ulcerative colitis. We are seeing today an occasional patient who has developed what is currently being called pseudomembraneous colitis from over-administration of antibiotics. Perhaps iatrogenic colitis would be a more suitable name. Too often we sit by expectantly while these patients die from devastating effects of pseudomembraneous colitis come by innocently through the over-administration of antibiotics. At postmortem, the colon is found to be a pus sac without mucous membrane. I think we should perform colectomy in such instances. Perhaps before next year's program, we shall hear reports of such patients whose lives were salvaged by colectomy.

We had such a case recently in which it would have been perfectly feasible to excise the colon restoring continuity. At postmortem, it was quite

evident that such a procedure might have been life saving. The advice, however, was not accepted. I have the feeling that presently such cases will be salvaged through timely operation. The other lesson—and probably the more important one, is to be careful in the use of any antibiotics which may lead to loss of the colic mucous membrane.

Concerning colostomy, I only wish I could share Dr. Lichtenstein's enthusiasm for cecostomy. As a prophylactic agency to prevent distention, carried out as an auxiliary to colectomy, I would agree: it can be very useful. Passage of the Grafton Smith tube at operation, however, which can be done in a few minutes, obviates in most instances the need for prophylactic cecostomy. Yet, I do use it, as Dr. Lichtenstein obviously does too.

When Dr. Lichtenstein says it is difficult to extrude the transverse colon, I am led to wonder whether he takes full advantage of the transverse abdominal incision in doing such a colostomy. When one puts a nickel on the umbilicus, as I suggested one do, and observes in the roentgen film first where the transverse colon is with reference to the nickel, it is easy to decide where to place the incision. Transverse colostomy is not only an operation upon the transverse colon; the incision also *must* be transverse, through which incision the distended colon will prolapse; one does not need to lift the colon out; it comes out by itself through the transverse incision placed directly over the colon. Finally, the mesenteric edges of the bowel are approximated to the peritoneum; two glass rods are placed through the transverse mesocolon under the colon. Such a temporary colostomy diverts completely when opened, because the lateral pull of the 2 glass rods separates the orifices of the afferent and efferent segments.

With reference to the matter of multiple operations upon the colon for excision of malignancies, I think such ventures are becoming less frequent. I suspect there is no one here any longer who does a Mikulicz exteriorization operation upon the colon or the Lahey modification for malignancy of the right colon. In the right colon, almost invariably, one can make a primary end-to-end anastomosis in the presence of obstruction because rarely does the small intestine participate in the distention. If it does, the gas can be milked down and a shoe-string clamp can be placed above it. Distal to the obstruction, there is no distention. As Dr. Lichtenstein implied, in the left colon, it is not so easy to do this.

Moreover, some of us who have tried it have found that to do a primary colectomy for an obstruction on the left side of the colon with great distention pyramids the mortality. The experience of the University Hospitals, reported in some detail in my book on "Intestinal Obstructions" (1955), suggests quite definitely that one cannot do primary colectomy in the presence of acute obstruction on the right colon, without augmenting mortality.

Dr. Dennis, you may recall, reviewed the comparative mortalities of cecostomy and transverse colostomy for acute colic obstructions. There is a big difference. When Dr. Dennis made this study in 1944, there was quite a difference in favor of transverse colostomy—and so there is today too. Transverse colostomy can be done as an essentially aseptic operation.

I deplore the making of internal short-circuiting or drainage operations. Every few months, I take one down that someone has made.

When we operate to remove a malignancy, and a prior colostomy has been made for acute obstruction, I make it a fairly routine plan to remove the malignancy and the colostomy and make a primary anastomosis. We do quite extensive colectomies, in any case, for cancers distal to the hepatic flexure in one stage. In old people with marked arteriosclerosis, one needs to take special care to see that the mid and inferior hemorrhoidal arteries are adequate to nourish the bowel in low resections.

Moreover, I do not employ antibiotic preparation for colic resections. If one employs the closed anastomosis, one does not need it. If one makes a nice closed anastomosis, the operation can be done more safely, I think, without antibiotics than with an open anastomosis protected by antibiotics.

Some time ago, I made this same remark in another university clinic. At the C.P.C. later, the pathologist brought to the conference, from the recent records of that hospital, reports of several deaths of patients who had undergone antibiotic preparation of the colon preparatory to resection. Obviously, the hospital pathologist was utilizing the occasion to support his own point of view to win converts among the surgeons over to the use of closed anastomosis and the omission of use of antibiotics. The only preparation one needs prior to colectomy is to be certain that a critical orderly or nurse has cleaned the bowel out well with enemas.

Dr. Lichtenstein made several nice points in his paper concerning our disagreements. I would only say that if this were Utopia, he and I would certainly see eye to eye—at least when we appeared together in public before an audience. And, if we had more time now to discuss our differences, we probably might too.

INDICATIONS FOR PYLOROPLASTY, VAGOTOMY, GASTROENTEROSTOMY AND RESECTION*

WALTER C. BORNEMEIER, M.D.

Chicago, Ill.

A review of the indications for the various surgical procedures that can be done on the stomach is always in order. The indications for surgery on most of the organs of the human body are published in surgical texts and they remain the same year after year. This is not so with the stomach; differences of opinion are not only regional, but they are found in the same city, and the same hospital—frequently there is disagreement among men in the same group or clinic. A description of all of the operations that have been done and are being done on the stomach would fill many textbooks. All of the articles that have been published on this subject could compose a library in itself. In spite of this, it is probably well for us to pause occasionally and list the indications for each operation—at least it gives us a point from which an argument could start and healthful enlightening discussion could result.

Before any indications for surgery of the stomach are discussed, let us decide what is not an indication. The first clinical entity that is in itself not an indication for surgery is a peptic ulcer. We never operate upon a person because he has an ulcer; we operate only because a patient has complications of the ulcer—we treat only the complications.

Among the complications of an ulcer, the number one position must be given to carcinoma—even if one is of the opinion that no ulcer ever becomes malignant because it is a malignancy before it is an ulcer; the resemblance by x-ray could cause a diagnosis of ulcer. The dictum that an ulcer on the greater curvature is always carcinoma is a good one to follow. A lesion high on the lesser curvature may be carcinoma. In a patient with ulcer of the stomach one should not wait until *all* of the acid is gone before surgery is advised. If six weeks of good management does not change the contour, it is malignant. If blood does not disappear promptly on medical management, it is malignant.

The next complication is continued excessive secretion of acid gastric juice. The normal amount of acid gastric juice in the stomach is 60 c.c. If as much as 100 to 200 c.c. of acid gastric juice is found, the excess is due to an ulcer or causes the ulcer. If this excess of acid cannot be reduced promptly by good medical management, the ulcer will be chronic and eventually the patient should be considered a candidate for surgery.

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Pyloric obstruction is a clear complication which, if due to spasm, should not have surgery; if the obstruction is due to scar tissue, surgery is a must.

Perforation is an indication for surgery, but there are some differences of opinion as to what operation is indicated. The type of surgery should be determined by the surgeon after he has opened the abdomen, weighed the difficulty of the resection, knows the condition of the patient, and realizes the extent of his own surgical skill.

Hemorrhage is a complication of an ulcer in which surgery must be considered. As always, the indications for conservative treatment must be weighed against the indications for operative interference. Bleeding that recurs, or is intense, makes surgery mandatory.

Up to this point we have enumerated and discussed indications for surgery, generally. This paper is supposed to enumerate the indications for pyloroplasty,

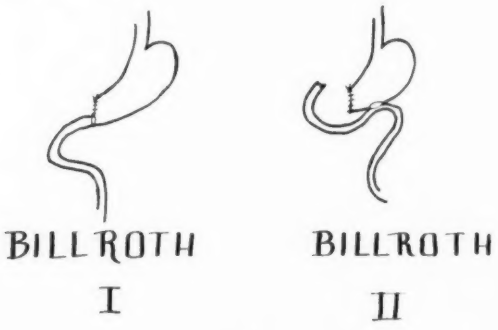

Fig. 1

vagotomy, gastroenterostomy, and resection. One can dispose of pyloroplasty rapidly by saying it is really only indicated in pyloric stenosis of the newborn. Here we often find the pyloric sphincter almost as firm as an iron band. Pyloroplasty has no place in the treatment of the complications of ulcer.

Gastroenterostomy can also be disposed of rapidly, for this operation by itself is indicated only where there is complete pyloric obstruction, not due to spasm. Its use with vagotomy will be discussed later.

We could quote volumes on the differences of opinion that have developed between the proponents and opponents of a vagotomy, but in a discussion of indications, it is hoped that the subject can be developed without need of arguments.

First we will review the types of gastric resection or partial resection that are commonly considered. In the Billroth I operation the antrum of the stomach

is resected (Fig. 1). The duodenum is brought up to the open end of the stomach. The Finsterer modification finds the side of the duodenum opened and anastomosed to the open end of the stomach (Fig 2). This Billroth I is indicated in a gastric ulcer which is prepyloric, occurring in the portion of the stomach which is removed.

The Billroth II operation finds about the same portion of the stomach removed, plus some of the duodenum if the ulcer is duodenal. The duodenum is closed; a loop of jejunum is brought up, either in front of the colon, or retrocolic through the mesentery of the transverse colon to be anastomosed to the open end of the stomach. The Billroth II, or one of the modifications, is the most common partial gastrectomy. The important points to consider in this procedure are: 1. the amount of stomach to resect, 2. the length of the remaining jejunal loop, 3. whether or not to close a portion of the gastric stoma before anastomosis, 4. whether or not to close all of the open end of the stomach--and

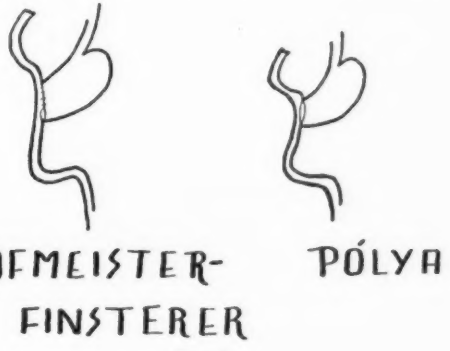

Fig. 2

making a new opening for the anastomosis, 5. whether or not to do an isoperistaltic anastomosis, 6. whether to bring the jejunum up through an opening in the mesocolon or bring it anterior to the colon. Thus it is easily seen that good or bad results of the operation depend on whether the proper resection was selected. Brandetsas[1] states, "I believe it may be a common fault of the average physician to assume that because a well-known internist or surgeon illustrates a method of management or a surgical technic, that the internist or surgeon concerned treats all patients with peptic ulcer disease in the same manner." He further observes, "the experienced internist, surgeon or general practitioner actually does much selection in choice of treatment for his patient." and his conclusion is "that the disinterested physician--may do harm by too insistent adherence to a proclaimed effective medical or surgical means of therapy." Perhaps some of the poor results *are* due to insistent adherence to a proclaimed means of therapy.

Let us consider the six most common points of operative variation. The amount of stomach to be resected is important. Certainly all of the gastric antrum should be resected. Dragstedt and Oberhelman[2] have reported in detail their work on the results of the stimulation of the gastric antrum, either left *in situ* or made into a pouch. Stasis of food or almost any stimulation by foreign material causes it to initiate the antral or humoral phase of gastric secretion with the resulting increase in gastric acidity. After removal of the antrum, one wonders how much can be accomplished by taking more. There seems to be a contest recently among different clinics and reports to see who can consistently remove the most stomach. Simultaneously, there appear more and more reports of dumping syndrome, weight loss, gastric distress and dissatisfaction with resection. Excessive stomach removal may prevent recurrences, but it also causes anemias, weight loss, and other general added complications.

Fig. 3

I believe the removal of more and more of the stomach should be carefully re-evaluated.

The length of the jejunal loop seems to have been important and it is generally conceded that the upper jejunum can better tolerate the fresh food mixture and avoid marginal ulcer. Therefore a short loop is preferred.

Closure of a portion of the stomach before anastomosing the jejunum should not materially alter the size of the stoma unless too much of the opening is closed. The diameter of the jejunum determines the speed of emptying. An isoperistaltic arrangement of the anastomosis signifies that the greater curvature is fixed to the distal end of the jejunal opening. Depending on the angle of the resection of the stomach, this is either good or bad. No definite evidence pro or con could be found, yet this problem has been blamed for failures. The retrocolic route for bringing up the jejunum was originally considered best.

Recently, however, more and more antecolic procedures are done because the surgical site is more readily accessible in the event further surgery is needed. The conclusion to be drawn then would be that in addition to the correct patient, the correct operation must be done.

Welch[3] states: "In general terms a patient should be made to understand his ulcer diathesis and learn how to treat it before the operation is carried out. It might be stated parenthetically that a certain period of suffering before operation results in much more gratitude to the surgeon and fewer complaints after operation." My personal observation is that there is no group of patients as grateful as those upon whom I have done resection for peptic ulcer. I believe the failures have not been due to a mistake in the type of operation, but are due to a mistake in deciding to operate. Patients with problems other than ulcer are not cured of their other problems by the surgery. Sometimes one wishes he had known the patient well for six months before consenting to do a resection or any kind of surgery to cure an ulcer that had become chronic.

In my opinion, for either a duodenal or gastric ulcer, a resection of 50 per cent to 75 per cent of the stomach which includes all of the antrum, is unsurpassed. I prefer a short loop, isoperistaltic antecolic gastrojejunostomy.

One operation that deserves mention is Bancroft's modification of the Devine pyloric occlusion. I believe this operation was devised before the function of the antrum was as well understood as it is today. Certainly, when Bancroft[4] described it, in 1932, he did not have the benefit of the work of Oberhelman and Dragstedt[2]. The operation has been modified since his description. On my service we use a further modification plus a simplification of the technic which makes the operation easier. The stomach is cut across about 3 to 4 cm. prepyloric, after ligating blood vessels from the pyloric sphincter up to the incisura on the lesser curvature, and up to the usual avascular area on the greater curvature (Fig. 3). By grasping the serosa and muscularis of the open distal segment with four Allis forceps, the upper one-half centimeter of mucosa is freed by sharp dissection. A Kocher clamp is then used to grasp this cuff of mucosa and with a gauze sponge this seromuscular area can then be wiped down as it inverts itself over the duodenum. Bleeding is almost entirely eliminated. When the pyloric sphincter is encountered, the separation is complete. A suture through the mucosa, tied firmly at sphincter level, permits the gastric antral remnant to be cut away. The seromuscular cuff is again brought up to its original position as an empty cone and can be easily closed. The stomach can then be resected as high as one needs and a gastrojejunostomy is done. The advantages of this operation, which works well in duodenal ulcer, are that the duodenum does not need to be mobilized in those instances where there is so much induration or swelling that good closure would be difficult, or where the ulcer is near the common duct. It is an easy operation and fulfills the requirement of removal of the antral mucosa, which if left intact and

exposed only to the alkaline duodenal content would be constantly screaming for acid; the humoral phase of gastric secretion would never be relieved and marginal ulcers, regurgitation of gastric juice and all of the uncomfortable complications would ensue. These then are the most common modifications of the Billroth II operation, indicated in carcinoma and all peptic ulcers.

Let us go back for a moment to the Billroth I operation, which was almost completely abandoned, but recently appears more and more in the literature[11]. It seems to be more physiologic in that "restoration of gastroduodenal continuity assures optimal flow of bile and pancreatic juice and the best possible mixing of food with these secretions, resulting in better utilization of fat" according to Schmitz et al[5]. They report 91 per cent satisfactory results. My impression, from reading the reports of Billroth I operations, is that in this operation excessive amounts of stomach are not removed. This fits the previously advanced theory that removal of an excessive amount of stomach is responsible for the present day epidemic of complications. The Billroth I is a good operation for gastric ulcer where the duodenum can be freed easily and brought up to the mobilized gastric remnant.

Finally, let us proceed to a consideration of the very controversial vagotomy. Most surgeons concede that vagotomy alone has not proven itself to be a good operation. Combined with a gastroenterostomy in duodenal ulcer it is a good operation. The jejunum must be anastomosed low down on the antrum in order not to initiate the humoral phase of gastric secretion. If it is true as Oberhelman and Dragstedt[2] point out, that "duodenal ulcers are usually caused by a hypersecretion of gastric juice of nervous origin and that gastric ulcers are usually due to a hypersecretion of gastric juice of humoral or hormonal origin" an anastomosis too high up would tend toward the development of a gastric ulcer[10]. Many surgeons report a large series where vagotomy is combined with gastroenterostomy. Holt and Robinson[6] found 87 per cent satisfactory results. Jakovljevic and Aleksic[7] from Yugoslavia, report 96 per cent excellent results. Still others report satisfactory results as low as 63 per cent[8].

Gastric resection has had its day and is still a very excellent operation. Vagotomy combined with gastroenterostomy has been given an excellent trial with both good and poor results. Now there is appearing in the literature an increasing large series of vagotomy combined with conservative gastric resection. The results appear to be good. Bolman and Lloyd[9] summarize that since recurrences following resection depend on the presence of intact vagi, and the recurrences following vagotomy depend on the presence of the antrum, conservative (50 per cent) gastric resection combined with vagotomy appears to be the operation of choice in the treatment of duodenal ulcer. This appears to be good reasoning.

In conclusion the preferred treatment for carcinoma is resection. The Billroth I operation works well in gastric ulcer. Conservative resection with

vagotomy seems to be a good operation for duodenal ulcer. This would be a good trio to start with, modifications as indicated, the right patient, and the right operation are necessary for good results.

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A REVIEW OF THE EFFECTS OF HORMONES ON SECRETION OF PEPSIN*

I. B. FRITZ, Ph.D.†

Chicago, Ill.

It has been known for many years that patients with adrenal insufficiency may have gastrointestinal impairments which can consist of anorexia, nausea, vomiting, abdominal pain and achlorhydria with achylia[1]. While these changes occur most frequently in acute adrenal insufficiency, they can also occur to varying degrees in chronic adrenal insufficiency. On the other hand, peptic ulcer incidence is low in Addisonian patients and in adrenalectomized animals. With this set of original findings lying dormant in the literature for many years, several different laboratories have recently done work in a systematic fashion on the interrelationship of adrenal-cortical hormones and gastrointestinal physiology. Baker and Abrams[2] have also worked with possible interrelationships with other hormones, and various workers[3,4,5] have been concerned with the possible protective action offered by adrenalectomy against gastric ulcer formation. The following paper is an attempt to review some of the salient facts which have been obtained during the past few years by various laboratories relating to the effects of hormones on gastric secretion.

Baker et al[2,6,7] have recently shown that hypophysectomy in rats is followed by an involution of the gastric zymogenic cells accompanied by an 80 per cent reduction in pepsin secretion during a six-hour interval following pyloric ligation. In an attempt to see which target glands are responsible for this effect, these workers did separate studies with gonadectomized, thyroidectomized and/or adrenalectomized animals. Using as a criterion the amount of pepsin secreted during a six-hour interval following pyloric ligation, they observed that gonadectomy had no effect upon gastric secretion. After thyroidectomy, the volume of gastric juice secreted was diminished, but the concentration of pepsin activity per milliliter of gastric juice was within normal levels. Consequently, it was concluded that while total pepsin activity was diminished because of a decreased volume of gastric juice secreted, there was no basic impairment in the mechanism of pepsin secretion following thyroidectomy.

In further experiments, Baker et al[2,6,7] found that either after adrenalectomy, or after combined gonadectomy, thyroidectomy, and adrenalectomy, comparable changes to those observed after hypophysectomy were obtained. They therefore concluded that the deficiency established by hypophysectomy

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†Presently at the Department of Physiology, University of Michigan, Ann Arbor, Mich.

which resulted in an impaired secretion of gastric juice and elaboration of pepsin resulted primarily from decreased adrenal-cortical activity. The changes which occurred following hypophysectomy or adrenalectomy included a marked reduction in the size of the gastric zymogenic cells, and a large reduction in the number of pepsinogen granules, evident histologically. The extent of these changes increased in severity from the time of removal of the hypophysis or adrenal until approximately three weeks postoperatively, at which time new conditions of gastric secretion tended to be stabilized. Correlated with these histological changes were functional changes of gastric secretion, in which the total amount of pepsin liberated was severely reduced. Concomitantly, the cell content of cytoplasmic ribonucleic acid was diminished. It was therefore postulated that this was another manifestation of low protein synthesis accompanying the decreased pepsinogen granules, and that the end result was a lowered pepsin production[6]. Implicit in these facts is the hypothesis that the mechanism of reduced pepsin secretion following hypophysectomy is associated with an impaired rate of protein synthesis, possibly resulting from a deficient formation of cytoplasmic ribonucleic acid.

After adrenalectomy, the volume of gastric juice was reduced insignificantly, but the activity of pepsin per milliliter was reduced from 99 x 10^{-4} pepsin units to 76 x 10^{-4} pepsin units, measured against the protein hemoglobin. Administration of 1 per cent sodium chloride in the drinking water to adrenalectomized rats did not significantly alter the effect. The *total* amount of pepsin secreted in a six-hour period by the gastric mucosa from normal rats was 1,200-1,530 pepsin units. After hypophysectomy this total was reduced to 325 pepsin units in a comparable time period. After adrenalectomy, however, this was reduced only to 731 pepsin units. The administration of whole adrenal-cortical extract to adrenalectomized and hypophysectomized rats partially restored pepsin activity to normal limits. This agrees well with the observation by Gray et al[4] that injection of ACTH or cortisone in man increases the peptic activity of gastric juice, and also increases the excretion of uropepsin.

The status of the thyroid gland's role as a possible regulator of pepsin secretion is less clear. Abrams and Baker[6] reported that in approximately half of their thyroidectomized animals, there was a slight reduction in size of the zymogen cells, and a pronounced decrease in both the number of pepsinogen granules and in the amount of cytoplasmic ribonucleic acid. In these animals that were affected, the extent of the loss of pepsinogen granules, the degree of basophilia and the variable loss of the size of chief cells was comparable in extent to that induced by hypophysectomy.

The reason why only half of the thyroidectomized rats displayed this phenomenon is not known. Sun and co-workers[8] have indicated the contradictory evidence in the literature on the status of gastric secretion in hypothyroid and hyperthyroid patients. In an attempt to delineate this problem,

they produced hypothyroidism in one of three ways: surgical removal of the thyroid and parathyroids of rats; administration of I^{131} to partially thyroidectomized animals; or administration of thiouracil to rats. Their results clearly show that surgical thyroidectomy is followed by a marked decrease in the rate of gastric secretion and in the total acid output. This, however, was not accompanied by any decrease in the pepsin concentration per milliliter of gastric juice. In fact, the pepsin concentration seemed to rise slightly. No correlation was found between the serum cholesterol, blood calcium or phosphorus with the total acid output and gastric secretion by the thyroidectomized animals. The only consistent finding in this regard was that the longer and greater the degree of hypothyroidism, the more pronounced were the effects on inhibition of gastric secretion and acid output. While thyroidectomy-induced hypothyroidism did not result in a lowering of pepsin concentration in gastric juice, it appeared from the data of these workers that the thiouracil and I^{131}-induced hypothyroid rats did show a decreased pepsin concentration as well as a decreased gastric secretion. Many possible factors exist which might account for the various reports that hypothyroidism may or may not be associated with an impairment in pepsin production. If hypothyroidism resulted in a true reduction of pepsin secretion, this action could be masked if excessive adrenal-cortical steroids were produced, resulting in an elevated pepsin production. One must therefore know the status of the adrenal-cortex in these thyroidectomized rats. The possibility exists that the production of hypothyroidism by pharmacological means results in a less pronounced hyperadrenal-cortical function than does the production of hypothyroidism by surgical ablation of the gland. Furthermore, it may be that I^{131} treatment or thiouracil treatment destroys only portions of the thyroid gland and allows certain thyroid products to be liberated, which may actually inhibit pepsin production.

At any rate, the interrelationship of the thyroid with pepsin production is not clear. One experiment that might clarify its role somewhat has not yet been performed. It would consist of observing gastric secretion and pepsin production in thyroidectomized, adrenalectomized animals maintained on constant physiological amounts of adrenal-cortical steroids. In this manner, it could be seen if the changes following thyroidectomy were independent of *increased* steroid production. It is well known that thyroidectomy is followed by adrenal-cortical hypertrophy. Varying degrees of overfunction of the adrenal may give rise to the conflicting results reported in the literature, since it is well established that adrenal steroids increase pepsin production. Until this type of experiment is done, the question whether thyroid hormone is required for optimal pepsin secretion must remain open, but the available data suggest that both thyroid and adrenal-cortical hormones play a role in the regulation of pepsin production.

An interesting observation was made by Cutting and co-workers[9] in 1937. They observed that after hypophysectomy in cats there was a decreased volume

of gastric juice secreted in response to various stimuli. This response, however, was not decreased if the neurohypophysis was left intact. It is therefore possible that various neural pathways, originating in some coordinating center, direct gastric secretion, but that the response is dependent upon a base line of minimal adrenal-cortical and thyroid hormones. This would fit in with the well known "permissive" action of adrenal-cortical steroids advocated by Ingle[10], since hypophysectomized animals would always contain small amounts of target gland products in spite of the absence of trophic hormones.

Interesting results have been reported by Gray and co-workers[4,5] on the significance of hormonal factors in the pathogenesis of peptic ulcer. They used uropepsin excretion as an index of pepsinogen release by zymogen cells. In order to use this index, Gray et al[4] had demonstrated that in the absence of a stomach there is no uropepsin excretion with or without the administration of ACTH. In intact animals, however, the administration of ACTH results in an immediate and sustained rise of uropepsin, sometimes going as high as 190 per cent higher than that prevailing before the administration of ACTH. It was estimated that uropepsin is approximately 1 per cent of the total gastric secretion, and it was repeatedly shown that patients with peptic ulcers have increased uropepsin excretion. Further, Gray and co-workers[4,5] demonstrated that the administration of ACTH (25mg./day intravenously) to normal patients resulted in uropepsin secretion as high or higher than that obtained in peptic ulcer patients. These authors stressed the fact that many nonspecific stresses could result in the elaboration of ACTH which in turn could elevate uropepsin secretion. These adrenal-cortical steroid effects were not blocked by vagotomy, by the various autonomic blocking agents such as Banthine or atropine, or by resection of the gastric antrum.

While patients suffering from Cushings' disease (hyperadrenal-cortical function) also show an elevated uropepsin secretion with or without ulcers, patients with hypopituitarism or hypoadrenal-corticalism, as in Simmond's and Addison's disease, have low uropepsin excretion. The administration of desoxycorticosterone acetate, testicular androgens, or estrogens have no effect on gastric secretion, pepsin or uropepsin production. Gray et al[4] also claimed that the only pituitary hormone that was effective in elevating the uropepsin excretion was ACTH. Thyrotropic, somatotropic, and gonadotropic hormones had no effects on uropepsin excretion, but the quantitative data are not recorded in their paper.

It has been shown by Haroutunian and Segal[3] that adrenalectomy offers some protection against gastric ulcer formation in the Shay rat. Earlier Selye[11] indicated that ulcers may occur as a manifestation of the shock phase of the alarm reaction to nonspecific stresses. It has also been shown that total HCl secretion is diminished after adrenalectomy, and it can be elevated by the administration of either whole adrenal-cortical extract or by the administration

of cortisone[3,12,13]. While Haroutunian and Segal[8] have shown that adrenalectomy offered almost complete protection to the Shay rat against rumenal ulceration, these authors pointed out that the ulceration could also be prevented by a host of other things, including vagotomy. Consequently, they caution against interpreting their data as indicating that adrenal-cortical steroids are essential for ulcer formation.

While all of the various papers cited to this point indicate the apparently close interrelationship between the level of adrenal-cortical hormones and the degree of gastric secretion and pepsin production, there is one paper by Davenport and Chavré[14] which demonstrates that in mice, adrenalectomy was not followed by a diminution of HCl secretion. The explanation for this discrepancy is not apparent, and one must fall back on the notion that perhaps there is a species difference, and that in the mouse, adrenal steroids are not directly involved with HCl formation. Davenport's contention, however, that previous workers[12,13] failed to control dietary and electrolyte factors in adrenalectomized animals must be considered.

Conclusions and Summary

The papers cited in this review strongly suggest that gastric secretion may be under hormonal regulation. After adrenalectomy and thyroidectomy, or hypophysectomy, there is marked inhibition of both the secretion of total gastric juice, and of the production and secretion of pepsin. The associated events which follow removal of these glands include a shrinking of the zymogenic cells, a diminution of pepsinogen granules, a decrease in cytoplasmic ribonucleic acid content, and a decreased pepsin secretion. This can be restored partially to normal by the administration of C-11 oxysteroids, but not with desoxycorticosterone. In fact, the excessive administration of C-11 oxysteroids or ACTH results in a greater than normal pepsin production and uropepsin excretion. There is some evidence which suggests that adrenalectomized animals are more resistant to the formation of peptic ulcers, and that organisms receiving excessive adrenal-cortical steroids are more susceptible either to the formation of new ulcers or to the perforation of previously existing ones.

It is a truism that the mechanism by which adrenal-cortical steroids and thyroid hormones affect pepsin production and secretion cannot be definitely elaborated until the mechanism of pepsin formation and release itself is better understood. In the meanwhile, it is equally obvious that the details of the interrelationship between these hormones and pepsin production need to be explored.

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NEW GASTROINTESTINAL AND URINARY SPASMOLYTIC DRUGS*

H. NECHELES, M.D., Ph.D., F.A.C.G.

N. C. JEFFERSON, M.D.

and

J. SPORN

Chicago, Ill.

We have had the chance to investigate a group of drugs experimentally on animals and therapeutically in man, that appear to us to have exceptional properties. Although these drugs are anticholinergic, we have not seen any patient among over 150 cases that had symptoms like blurred vision, dry mouth, or urinary retention. On the contrary, some cases with urinary retention were benefited remarkably by some of these drugs. Their degree of toxicity in animals and in man is of a small order. The structure of the compounds is demonstrated in Figure 1.

1. Dactil, N-ethyl-3-piperidyl-diphenylacetate-HCl.
2. Piptal, N-ethyl-3-piperidyl-benzilate methobromide.
3. Cantil, N-methyl-3-piperidyl-benzilate methobromide.
4. Tridal, a combination of 50 mg of Dactil and 5 mg of Piptal.

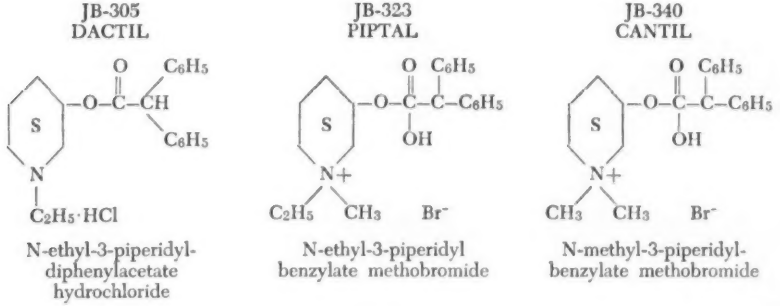

Fig. 1

RESULTS

Dactil, Piptal, and Cantil inhibited gastric and intestinal motility, stimulated with prostigmine, in trained, unanesthetized dogs, but salivation was not

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Department of Gastrointestinal Research, Medical Research Institute of Michael Reese Hospital, Chicago, Ill.

affected. In acute experiments on anesthetized dogs, Dactil proved to relax the sphincter of Oddi, and barium stimulated motility was inhibited with Piptal and Cantil.

Dactil:—Dactil has distinct surface anesthetic effects in addition to its anticholinergic effects. We have utilized this property in the treatment of cardiospasm in infants and adults[2]. Cardiospasm may be produced by distant reflexes from gallbladder, appendix, high gastric ulcers, etc., or by reflux of gastric juice into the esophagus. These disturbances may produce esophagitis and esophageal ulcers, which in turn would maintain the cardiospasm. A local anesthetic may abolish such local reflexes, and our clinical results with Dactil appear to support the above hypothesis. With oral administration, the effects

TABLE I

PIPTAL WITHOUT PHENOBARBITAL, SUMMARY

No. of Cases	No. of		Age		Dose in mg.	Effects of Piptal			
	Males	Females	Range	Average		0	+	++	+++
Duodenal Ulcer 2	2	—	46 & 49	48	5 mg. once t.i.d. or q.i.d. in all cases		1		1
Genitourinary Disease, Urinary Retention 8	5	3	21-54	42	Same	1	0	3	4

+++ Excellent Result, Complete relief
++ Good Result, Greatly relieved
+ Fair Result, Some relief
0 Failure, No relief

of the drug took place rapidly. In an infant with cardiospasm no barium entered the stomach for 30 minutes, while following Dactil, barium progressed into the stomach within less than 10 minutes. Good effects of Dactil noted by us in cases of diaphragmatic hernia may be explained on the same basis as in cardiospasm. In idiopathic hypertrophic pyloric stenosis in infants, Dactil had little or no effect. In biliary dyskinesia and spastic colon, good results were obtained in two-thirds of the cases. Spasm of the urinary bladder and the urinary sphincters was not affected by Dactil. This drug appears to be beneficial mainly in spasm of the upper gastrointestinal tract. No toxic or disturbing side reactions were noted in any of the patients receiving Dactil[1].

Piptal (JB 323):—(Table I.) Most of our own experience with Piptal was obtained from clinical cases with genitourinary disease and urinary retention. Of 6 patients with urinary retention 5 were benefited greatly. The one with

negative results was a case of prostatic hypertrophy and prostatism. Piptal (and JB 340) are the only anticholinergic drugs which, in our experience, do not tend to produce urinary retention, but which are able to abolish it in a surprising number of instances. In 3 patients with dysmenorrhea and pelvic inflammation, good to excellent relief was observed. In 2 patients with duodenal ulcer, fair and excellent results were obtained. No effects on the pupils or on salivation were noted in the patients treated with Piptal.

Tridal:—(Table II.) Tridal is a combination of 5 mg. of Piptal and 50 mg. of Dactil. This compound was made with the idea to combine the fast spasmolytic and topic anesthetic effects of Dactil with the stronger spasmolytic action of Piptal.

Of 26 cases of spastic colon, 25 were benefited greatly, and one case was refractory. Of 12 cases with ulcer syndrome, 8 were benefited greatly, and one case was refractory. All 4 cases of biliary disease were benefited greatly. The compound was remarkably effective in cases with urinary retention, all 5 cases obtaining efficient relief. In the summer and fall of this year (1955), Chicago experienced an epidemic of gastroenteritis, probably due to virus and bacterial infection. Cases with nausea, vomiting, abdominal cramps, diarrhea, and fever in some, were frequent. Diet, bed rest, antibiotics, etc., were slow in combating the symptoms. Tridal was very helpful in all 15 cases of this group, with immediate relief of nausea, cramps, and diarrhea in many of the patients.

The miscellaneous group consisted of one aged patient with hypertension, senile dementia, and epigastric distress, in whom Serpasil was ineffective. This patient improved with Tridal, the abdominal pain disappeared, and she felt better. The second patient came to the hospital with an acute anginal attack, after being found gasping in his car. Tridal with phenobarbital relieved him, and anginal pain disappeared. The third case was a male alcoholic, suffering from cardiospasm for 1 week who received Tridal with phenobarbital and was able to swallow solid foods without difficulty.

In the Tridal group, 3 cases, i.e. 3.7 per cent of side reactions were seen. One case with spastic colon, a 56-year old man, whose complaints were revealed at autopsy to have been due to cancer of the colon, received 4 tablets of the drug per day with phenobarbital. The abdominal pain subsided, but he reported palpitations of the heart 10 minutes after every dose of Tridal. One case with recurrent pelvic inflammatory disease reported one attack of weakness and dizziness following 1 tablet of Tridal. One male patient, 51 years of age, a neurotic with x-ray negative ulcer syndrome, had only slight relief with 1–2 tablets of Tridal q.i.d. and he reported periods of slight dizziness following taking of the drug. These were the only cases with side reactions occurring in our entire series of cases treated with Dactil, Piptal, Tridal and Cantil, a total of 123 cases, i.e. 2.4 per cent.

TABLE II

TRIDAL SERIES, SUMMARY

			Age		No. of Cases		Effects of Tridal				Side-effects	
No. of Cases	Males	Females	Range	Average	Tridal	Tridal + Phenobarbital	0	+	++	+++	No.	Nature
Spastic Colon 26	10	16	17-62	42	13	13	1	0	9	16	1	Palpitations
Genitourinary Disease 17	–	17	22-45	32	12	5	1	0	8	8	1	Weak & dizzy once
With Urinary Retention 5	–	5	27-33	31	5	–	0	0	2	3	None	
Biliary Disease 4	1	3	40-63	49	2	2	0	0	2	2	None	
Ulcer Syndrome 12	6	6	18-52	41	3	9	1	3	1	7	1	Slight dizziness for few hours
Gastroenteritis 15	7	8	10-55	34	10	5	0	0	7	8	None	
Miscellaneous 3	1	2			1	2	0	0	3	4	None	
82	25	57			46	36	3	3	34	46	3	3.7%

Cantil (JB 340):—(Table III.) This drug was used in 30 cases, 18 with spastic colon, 4 with biliary disease, 2 with ulcer syndrome, and 6 with genitourinary disease. Side reactions to 340 were not observed. In the 4 cases with biliary tract disease, i.e., cholecystitis and dyskinesia, good results were obtained. Likewise, one case with duodenal ulcer and one with gastritis were benefited greatly. Among 18 cases with spastic colon, negative results were obtained in one case, good to excellent results in 17. In 6 cases with dysuria, dysmenorrhea, and postoperative retention, good to excellent results were obtained in 5 cases, a fair result in one case with pelvic inflammation.

In motility experiments in trained unanesthetized dogs, small doses, 1-2 mg i.v. of 340 depressed stomach and colon motility considerably for prolonged periods of time. Colon motility was inhibited more than stomach motility in most tests. This observation is supported by good clinical results obtained in the cases with spastic colon.

TABLE III

CANTIL WITHOUT PHENOBARBITAL, SUMMARY

No. of Cases	No. of		Age		Dose in mg.	Effects of Cantil			
	Males	Females	Range	Average		0	+	++	+++
Biliary Disease 4	—	4	36-49	43	5-25 mg. t.i.d. or q.i.d.	0	0	2	2
Ulcer Syndrome 2		2	23 & 52	38	10 & 25 mg. t.i.d. & q.i.d	0	0	1	1
Spastic Colon 18	5	13	17-69	41	5-25 mg. t.i.d. & q.i.d	1	0	7	10
Genitourinary Disease 6	2	4	16-72	40	5-25 mg. t.i.d. & q.i.d.	0	1	2	3

COMMENT

We have described 3 new spasmolytic drugs of the class of piperidyl compounds, which have demonstrated new features in the therapy of gastrointestinal spasm. With oral administration, all of them have a low degree of toxicity, a relatively fast onset of action, and complete absence of urinary retention. Piptal and 340 had in addition urinary spasmolytic effects. To us, this is a unique property of spasmolytic drugs, because the known strong anticholinergic drugs may at times produce troublesome urinary retention.

The combination of anticholinergic and surface anesthetic effects in Dactil may prove to be an important factor in the treatment of upper gastrointestinal tract disease. The combination of Dactil and Piptal may be more widely effective because the distinct anticholinergic properties of Piptal, together with the topic anesthetic action of Dactil may be beneficial in more generalized spasmolytic effects than either drug by itself. The greater effect of Cantil on the colon than on the stomach may suggest its usefulness in conditions associated with lower intestinal spastic conditions.

Side reactions were not encountered with Dactil, Piptal, or Cantil, but with the Dactil-Piptal combination, Tridal, 3 side reactions were observed among 82 patients, i.e. 3.7 per cent.

While our results are encouraging, further clinical evidence will establish the place of these drugs in therapy.

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Discussion

Dr. N. C. Jefferson (Chicago, Ill.):—I would like to make one or two supplementary comments regarding our work and observations, both experimentally and clinically, with the use of these piperidyl compounds.

First I should like to say that one case was so outstanding, I believe I should mention it in a little more detail. We have, in our hospital, a paralytic who received his spinal injury in Boston five years ago. At that time he remained in a Boston hospital for two years. He has been with us, hospitalized now for three years, under the care of a urologist because of the bladder and rectal condition; in other words, he is unable to have spontaneous B.M.'s; he is unable to pass gas or to void. For that reason, he is maintained constantly with a catheter of the Foley type. The urologist removes the catheter once a week in order to allow him a period of a few hours rest. On attempts to reinsert the catheter, up until the last seven or eight months, a period of approximately one to one and one-half hours was required to replace the catheter.

We used Piptal, in 5 mg. doses, with this patient, and the urologist was then able to replace the catheter in a period of about ten minutes. Moreover, the patient then began to be able to expel gas voluntarily from the bowel, but is yet not able to have spontaneous bowel movement. He still has to have a low enema. The patient, of course, is happy about this drug. We have studied the blood picture to see if the prolonged use of the drug would alter or have any effects upon it, so far there have been none observed.

The second thing I would like to mention would be the use of Cantil, the latest piperidyl drug, which is not on the market yet. We began to use this drug in 10 mg. doses, and we are now using it in 25 mg. doses. The effects, in applicable cases, are really dramatic.

In doing rectal surgery and surgery around the inguinal region for hernia, especially with the use of spinal anesthesia, almost equally in males and females many patients get a postoperative urinary retention. It is dramatic how you can give one tablet of Piptal, or Cantil, and this retention is usually immediately relieved without further need of more medication. We know all too well that, if these patients have to be catheterized, it is usually necessary to catheterize them more than once. This morning I just completed a Whitehead rectal operation, and I left the Cantil at the bedside because I suspect we will get a retention and, as soon as we do, we will start the Cantil.

I think those are a few supplementary observations that might be added to the dissertation that has been made by our chief and director of Gastrointestinal Research at Michael Reese, Dr. Necheles.

Dr. Harry A. Oberhelman (Chicago, Ill.):—I must admit that the last two papers are far beyond my ability to discuss. I shall, however, limit my remarks to the paper presented by Dr. Bornemeier.

I want to apologize for pinch-hitting for Dr. Wangensteen. I know that he has a fund of knowledge to impart to everyone. I am pleased that I may express my loyalty to some of the older established methods of gastric surgery which I believe to be safer in the hands of the greatest number of surgeons. The procedure that Dr. Wangensteen has outlined to you entails, I believe, a good deal more technical procedure than we are ordinarily accustomed to in our gastric surgery. If you feel that it is a little beyond the scope of your ability as a surgeon to successfully execute such an operation, it might be well that you stick to some of the more established methods.

It is, however, through such procedures as Dr. Wangensteen has outlined, that progress is made. Until it becomes a procedure universally accepted, I think it is safe for us to continue with some of our established procedures.

I think Dr. Bornemeier covered this subject very well. I cannot criticize his procedure, and I am not going to do so.

In the first place, when we select patients for surgery, I want to reemphasize that we must select them very carefully. In my internship days with the late Dr. Dean Lewis back in 1921 and 1922, gastroenterostomies then were becoming quite popular. Every ulcer patient that came to the surgeon was treated by a gastroenterostomy. The surgeons soon learned that just because there was an ulcer the patient sooner or later got into serious difficulty. It wasn't long until the universal gastroenterostomy for peptic ulcer was abandoned.

If you are going to operate a patient for peptic ulcer, as Dr. Bornemeier said, we don't do surgery for the ulcer, we do surgery for the complications of ulcer.

One thing that I have recognized in recent years, and I am very glad to see that our medical colleagues are assuming a slightly more tolerant attitude toward these complications: B. W. Sippy's indication for surgery in addition to perforation was obstruction, and it had to be pretty severe, probably 60 to 70 per cent retention overnight. Hemorrhage and repeated hemorrhage was not considered in those days as a surgical indication. Persistent pain was not accepted in those days as an indication. In recent years, however, which has been very encouraging to me, both internist and surgeon have assumed a more sensible attitude. These conditions that years ago were not considered surgical indications are now so considered. It has taken some years to convince some of our colleagues of that fact. They have seen good results that have been obtained by surgery in patients with recurrent hemorrhages, or intractable pain.

I want to say one word about gastric ulcer. We have been told by some of our leading surgeons in the United States, that every gastric ulcer in an individual of 40 years or over is surgical. Now, that is taking a rather dogmatic attitude. It seems to me not quite logical. This concept was based on the idea that many of these ulcers were precancerous. In more recent years, statistics reveal that only a small percentage of these ulcers are precancerous.

I was very glad, a few years ago, to hear the late Dr. Frank Lahey discuss the surgical treatment of gastric ulcer. He had at one time said, and shared the view, that all gastric ulcers in people over 40 were surgical lesions. He later modified that view. All gastric ulcer patients seen for the first time, he stated were entitled to two or three or four weeks of accurate, careful ulcer management. He further said, that if there is a very appreciable healing of the lesion, as revealed by x-ray, one may rest assured that one is not dealing with any precancerous lesion.

He said, "Those cases that we at one time placed in the surgical category, we now have shifted over into the medical category."

I think that is pretty sound reasoning. I have adopted the view in the last four or five years, that, if our patients respond to medical management in gastric ulcers, we should give them the benefit of medical management. You may say they will recur. In these ulcers that tend to recur conservative management should be abandoned and surgery substituted. It means that one must select his patient carefully, for surgical therapy.

Now, as far as the bleeding ulcer is concerned, it sounds very simple: "Here is a man who is hemorrhaging, you had better operate on him and prevent death." It is not that simple. I think a persistent, uncontrolled gastric

or duodenal hemorrhage is probably one of the most perplexing and difficult conditions I know of to treat from a surgical standpoint. You can do no less in those cases than resect. That is a formidable procedure under critical circumstances. Fortunately, these do not happen very often. Most patients can be placed into the elective category.

Now, as far as the Bancroft operation is concerned, we like to speak of it as the exclusion operation, where the duodenal ulcer is left *in situ*. I think we as honest, let us say, ordinary surgeons will keep out of a lot of trouble if we pursue this method. The Bancroft procedure, where we leave a stump of the pylorus and excise the antral mucosa, has been advocated for a long time.

About four years ago, I said to my associates, "If that procedure is good where your ulcer has penetrated and is frozen to the head of the pancreas, why isn't it good all the time? Why resect any duodenal ulcers?"

We followed that procedure for several years. I must say we have found no ill effects, in spite of the fact that some of the leaders of our surgical thought today say that in those cases treated by the Bancroft method, you have a higher incidence of stomal ulcers, than in those cases where the ulcer has been resected.

Some of our leading surgeons in the country today, to avoid damage to the common bile duct, during gastric resection, suggest and advocate that you intubate the common bile duct to prevent injury to it. This formidable preliminary procedure is unnecessary when the Bancroft exclusion technic is employed.

I think we, as teachers in the surgical profession, should keep our feet on the ground and should advocate less complicated procedures. If you have an ulcer that is frozen to the head of the pancreas, for heaven's sake, do the Bancroft operation and let the ulcer alone. You will stay out of trouble, and your patient will get along very well.

Now, as far as vagotomy is concerned, I have had little or no experience with it. I have watched Dragstedt, and I have been impressed by his work.

We have attempted a few. I will be very frank with you that I am never sure I have cut all the fibers. I often wonder if every surgeon who does vagotomies is sure that he has gotten every fiber. Since our results with gastric resection have been gratifying, and it is a procedure that we are familiar with I have adhered to the subtotal gastric resection. I don't know how far one should go with resections. Some leave probably one-fifth or one-sixth of the stomach. I am not an advocate of such radical surgery. I think there is a happy medium.

Research studies conducted in the Department of Surgery of the University of Washington Medical School on the development of the antral cells, revealed that rarely did they find any such cells at a level higher than where

the left gastric artery enters the stomach. Their conclusion was, if you go up to that level, which includes about three-fifths of the stomach you have done an adequate resection.

As far as total resection is concerned in carcinoma of the stomach, we do almost a complete resection, only occasionally. That is a matter of personal opinion.

The conditions in which vagotomy is good, as Dr. Bornemeier said is in the group of cases where we are dealing with stomal ulcers, whether following gastric resection or following gastroenterostomy. Here vagotomy is the operation of choice. Yet when you have a patient with a stomal ulcer that has threatened to perforate, or has perforated probably into the transverse colon, you can't tell me that vagotomy is going to do the trick. You have to use mechanical means to dispose of the ulcer area, by resecting the stoma. You will have to resect a segment of jejunum and re-establish the continuity there and proceed as you did in the first place with the so-called Billroth II operation.

I am glad to discuss this subject with you and I hope I have hit the high points.

Dr. I. Snapper:—My old Chinese friend, Dr. Necheles, has given us hope that we can, perhaps, in the future expect an anticholinergic drug which does not cause spasm of the bladder. The possibility alone that in the near future we may have an anticholinergic preparation which will not evoke the syndrome of prostatism is very encouraging. Dr. Necheles has mentioned one of his drugs which relieved cardiospasm in a young child but disappointingly didn't act on pylorospasm. A child of ten months who has difficulty in swallowing, however, does not actually suffer from a spasm of the cardia. In such a case a bougie easily passes through the cardia. In the absence of spasm the name of cardiospasm should not be used in such patients but be replaced by the designation achalasia. This disease is caused by an imbalance of the innervation, by the absence of synergism between relaxation and peristalsis. In other cases an actual spasm of the cardia exists. I am sure that Dr. Winkelstein, in his discussion of ulceration of the esophagus, will mention conditions with actual spastic closure of the cardia where a bougie cannot pass easily. Thus, one could hardly expect that the same drug would be active both in achalasia which is no spasm, and in the pylorospasm which is caused by a genuine spastic contracture of the hypertrophic pyloric muscle.

I have listened with great interest to Dr. Fritz, but I wonder whether all the endocrine glands have to obey the wishes of the slavemaster, the anterior lobe of the pituitary.

As was already mentioned yesterday, peptic ulcer is frequently found in hyperparathyroidism. The function of the parathyroids is not influenced by the anterior lobe of the pituitary. In the etiology of this hyperparathyroid peptic

ulcer which is endocrine in nature, neither the anterior lobe of the pituitary nor the adrenal cortex seems to play a role.

I fully agree that the formation or exacerbation of peptic ulcer during corticosteroid treatment is not completely explained by the increased uropepsin excretion alone. ACTH certainly influences the reactions of the collagen tissue which must also change the course of a peptic ulcer. But, on the other hand, ACTH by increasing pepsin secretion alone without changing the HCl secretion, could well aggravate peptic ulceration.

The peptic activity of pepsin is strongest at the pH of normal gastric juice but is at least partly inhibited by hyperchlorhydria. Therefore, increase of uropepsin alone, without increase of hydrochloric acid, would just as well, if not better, explain the ulcers under the influence of ACTH than if ACTH would have increased both pepsin and hydrochloric acid secretion.

As far as surgery of peptic ulcer is concerned, we are apparently still in the stage where "from the shock of the opinions, the truth must spring forward."

We heard the recommendation of Dr. Bornemeier that the antrum had to be removed; we heard Dr. Wangensteen insist that the antrum be saved during the operation.

We do not want to rush in where angels fear to tread. All of us have seen ulcer patients who were resistant to medical treatment but did extremely well after operation. But this is not always the case. A certain percentage of ulcer patients is not helped by surgical procedures. We *hope* that this percentage has decreased, thanks to modern technics.

Dr. H. Necheles:—Gentlemen, I would like to say a few words about uropepsin, because I am afraid that the situation is not entirely clear, and that we may go overboard with the application of uropepsin in diagnosis.

I was very glad to hear what Dr. Snapper and what Dr. Fritz said. Both warned that we don't know enough yet. The first thing with uropepsin or any method that tries to establish values, we should know about the normal values. We have done that. We find, first, that there is a great difference in sex. The female is always lower in uropepsin. The child is low in uropepsin. Above 60 years of age, the uropepsin drops considerably. This has to be considered in statistics and was not before.

Second, uropepsin in ulcer. We have studied patients with no digestive complaints, normal subjects with no digestive complaints whatsoever, completely normal persons, and an equal group with active duodenal ulcer, proved clinically and by x-ray. In both of the groups, beyond any question of doubt, the uropepsin excretion in the urine was the same. The only difference was that this work was done in a prison where prisoners, contrary to usual belief, do not

lead an easy, carefree life, but where there is a great degree of tension and upheaval all the time.

So here you had two groups. Both of them had high uropepsin values compared with people outside the prison. One group had active ulcers; the other group had none. This demonstrates that uropepsin does not indicate ulcer, that it indicates a certain stress.

I want to refer to Dr. Gray's work, which he did not stress when he talked here, namely that, with physical and mental stress, the uropepsin excretion is much greater than in the average ulcer patient.

Third, with Dr. Sorter, we have tested uropepsin excretion in a group of six aged women in a home for the aged. We have given them, over many weeks, between 50 and 150 mg. of cortisone per day, and we have found an increase in uropepsin excretion in only one of these women.

This woman, interestingly, had a history of duodenal ulcer healed. She had a low uropepsin before of 120 and, with cortisone, it increased to about 250, a high increase but within the limits of normal that we had found before. There were no signs in this woman of any activation of her ulcer. She was watched, of course, very carefully.

Therefore, also in an aged person there may be an exception to the usual increase in uropepsin with duodenal ulcer.

So, I want to impress upon you that this work is still in the experimental stage. I want to tell you not to use it as a diagnostic tool for the diagnosis of duodenal ulcer.

CARCINOMA OF THE STOMACH*

A Need for Earlier Diagnosis

ALTON OCHSNER, M.D.†

and

JOHN BLALOCK, M.D.†

New Orleans, La.

There are probably few if any cancers which occur so commonly as gastric cancer and yet are associated with such a poor prognosis. Tremendous advances in the diagnosis and therapy of all cancers have been made in the past decade with the possible exception of gastric carcinoma. The poor results in the treatment of cancer of the stomach cannot be attributed to the fact that it is a new disease, as is the case of cancer of the lung, because gastric cancer has been a common disease since the time of the ancients. A review of reported statistics from the better institutions in the United States shows that the five-year survival rates of all patients with gastric cancer admitted to the insitutions vary from approximately 1 per cent[1] to 14 per cent[2,3]. In all the cases of gastric cancer in the metropolitan area of Houston reported by Clark[4] there was a five-year survival rate of only 0.8 per cent.

Carcinoma of the stomach is second in frequency in men to cancer of the lung and comprises 18 per cent of all cancers[5]. According to Steigmann[6] 40,000 persons die annually from cancer of the stomach in the United States and this has increased from 26,215 in 1948, an increase of 52 per cent. In 1948, there were 17.9 deaths from cancer of the stomach per 100,000 population and this increased to 53.7 in 1953[7].

Berkson et al[2] report that one in every 200 patients admitted to the Mayo Clinic has a malignant lesion in the stomach. In the Ochsner Clinic[8] the incidence was one in every 588 admissions. In the Charity Hospital in New Orleans[9], a gastric cancer was found in every 265 admissions.

Because of the tremendous number of cases of gastric cancer and because of the uniformly poor results which are obtained in its treatment, it is essential that the medical profession reevaluate the problem and undertake steps to improve the results. We are convinced that this can be accomplished only by earlier diagnosis. Although there has been considerable controversy concerning the best way to improve the results, many believing that more radical surgical procedures such as total gastrectomy in all cases of gastric cancer are necessary, from our experience we are convinced that only by earlier diagnosis and earlier

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†From the Department of Surgery, School of Medicine, Tulane University, and the Ochsner Clinic, New Orleans, La.

institution of curative therapy can the cures be increased. Obviously, in the treatment of any malignant lesion, it is necessary to remove all the neoplastic disease, and this necessitates removing most of the viscus involved. On the other hand, we are convinced, after considerable experience, that with the exceptions of lesions located in the proximal portion of the stomach and infiltrative lesions, such as *linitis plastica*, total gastrectomy is not necessary to obtain the best results and we are equally convinced that when a radical subtotal gastrectomy is done, the functional results are much better than following a total resection of the stomach. Were it not for the latter fact, total gastrectomy might be considered as a routine procedure in all patients with gastric cancer. Because, however, individuals subjected to complete removal of the stomach frequently are incapacitated by persistent distressing digestive symptoms and in reality are digestive cripples, this operation is to be avoided unless the malignant lesion cannot be removed completely in any other way.

In discussing an operative procedure short of total resection of a viscus, it is necessary to define what is meant by that procedure. This is particularly true in the case of gastric cancer, because from reported statistics, gastric resection for cancer apparently means anything from a "biopsy" to a good cancer operation. McNeer and his coworkers[10] reported the autopsy results in 92 patients who had previously been subjected to resection of the stomach for gastric cancer. In 46 (50 per cent) there was local recurrence of carcinoma within varying periods of time from two to 75 months after the gastrectomy either at the gastroenterostomy site or in the wall of the stomach. In 60 cases in which it was possible to determine the extent of the resection which had been performed, there was no local recurrence in 16 and local recurrence in 44. Of the 16 with no local recurrence four (25 per cent) had less than 25 per cent of the stomach resected, four (25 per cent) had one-half resected, seven (43.8 per cent) had from one-half to three-fourths resected, and only one (6.3 per cent) had more than three-fourths of the stomach resected. Of the 44 with local recurrence seven (15.9 per cent) had less than one-fourth resected, 15 (34.1 per cent) had one-half resected, 20 (45.5 per cent) had from one-half to three-fourths resected, and only two (4.5 per cent) had more than three-fourths of the stomach resected. It is worthy of note that only four of the 60 patients had more than 75 per cent of the stomach removed and it is understandable why there was such a high incidence of recurrence in the remaining portions of the viscus.

As mentioned previously, we are convinced that radical subtotal removal of the stomach and *en bloc* removal of the regional lymph nodes will give the best results in the treatment of most cancers of the stomach and that it is unnecessary to resort to removal of the entire stomach except in the invasive type of cancer and the case in which the cancer is located in the proximal portion of the stomach. The radical subtotal resection of the stomach which we

perform consists of excision of the first portion of the duodenum because of the frequency of involvement of this area, all of the lesser curvature of the stomach up to the esophagus, all of the greater curvature of the stomach to within 5 to 6 cm. of the esophagus, the *en bloc* excision of the gastrohepatic omentum, the gastrocolic omentum, the greater omentum, and the following lymph nodes: those along the lesser curvature especially around the celiac axis and the left gastric vessels, the subpyloric nodes, the subhepatic nodes including the nodes in the hepatic pedicle, the gastrolineal nodes, the retropancreaticoduodenal nodes, and the paraesophageal nodes. The spleen is also removed as an *en bloc* procedure. The duodenal stump is closed blindly, the upper portion of the small gastric pouch is closed, and the inferior portion is used to anastomose with the side of the jejunum which usually is brought up through the transverse mesocolon. The remaining gastric pouch which is usually no larger than a man's thumb and the remaining few intact left vagus fibers are responsible, we believe, for the paucity of symptoms which these patients have in contradistinction to the usually marked symptoms of which patients who have been subjected to total gastrectomy complain. We are of the opinion that the remaining pouch is of less significance than the persistence of the left vagus fibers in the prevention of postoperative symptoms.

Although in the past many patients with gastric cancer have not had the advantage of radical resection, there have been many in whom an adequate radical procedure has been used and yet the results in the treatment of cancer have not been as good as is desired. It is obvious, therefore, that the results can be improved only by subjecting the patient to an adequate surgical procedure at a time when the lesion is still limited to the stomach. As mentioned previously, the over-all five-year survival rate in the reported series is from 1 to 14 per cent, whereas in a series of cases in which there is no lymph node involvement, in most of which the lesion is limited to the stomach, the five-year survival rate varies from 26.9 per cent[11] to 56 per cent[12]. The five-year survival rate in our cases in which there was no lymph node involvement was 57 per cent[8].

Although the statement is frequently made that carcinoma of the stomach is easily diagnosed, it is a fallacious statement, because although the diagnosis is easy in the later stages of the disease, it is extremely difficult early in the course of its development. It is a common concept that cancer of the stomach is diagnosable by x-ray in well over 85 per cent of cases. We are of the opinion, however, that a gastric lesion which is diagnosable by x-ray as gastric cancer is frequently so far advanced that cure is impossible. All too frequently the clinician is unwilling to make a diagnosis of cancer of the stomach until there is roentgenologic evidence of the lesion which is hazardous, because, if the results in gastric cancer are to be improved, it is necessary that treatment be instituted at a time when the malignant lesion cannot be diagnosed as such. By this is meant that in order to improve the results in gastric cancer it is necessary

to treat conditions which are clinically not cancer but which mimic cancer or may be even precancerous lesions.

We believe that all gastric ulcers should be treated surgically and that the physician who institutes the conservative treatment of an ulcerative lesion of the stomach assumes a tremendous responsibility. In many cases it is impossible by any means whatsoever, except by careful microscopic examination of the lesion, to determine whether the lesion is malignant or not. Although there is some difference of opinion concerning the possibility of a benign ulcerative lesion of the stomach undergoing malignant change, it is our belief that such can and does occur. In addition to the impossibility of differentiating benign from malignant ulcerative lesions of the stomach, another advantage of surgical removal of all gastric ulcers is that the results are better than with the conservative treatment. Cain et al[13] found that the results from the nonsurgical treatment of gastric ulcers were not good. In 336 patients in whom medical therapy was started and considered to be the best method of treatment, the lesion was found to be malignant in 33 (9.8 per cent). In 140 patients in whom medical therapy was originally used but subsequently abandoned for surgical therapy, 34 (24.3 per cent) were found to have cancer. They conclude that an individual 40 years of age with a gastric ulcer has 100 times more chance of having a gastric cancer than does the general population. Hayes[14] studied 899 cases with peptic ulcer symptoms at Yale University of which 472 were diagnosed as having malignant lesions and 427 were diagnosed as undoubtedly benign. Of these cases diagnosed as benign lesions, 106 were operated upon after no more than four weeks of conservative therapy and 56 (28.6 per cent) were found to be cancer. It can therefore be stated conservatively that at least 10 per cent of all gastric ulcers are malignant, that it is impossible to differentiate benign and malignant ulcerative lesions without microscopic examination, and since the mortality following gastric resection for such lesions is definitely less than one per cent, the physician who advises conservative therapy and watchful waiting policy in the treatment of gastric ulcer assumes a hazardous responsibility. Although a physician may be reluctant to suggest a subtotal gastric resection for all gastric ulcers, which we believe is the method of choice in the treatment of these cases, it is essential that at least the entire ulcer be extirpated and the lesion subjected to careful microscopic examination to determine whether it is neoplastic or not.

In addition to gastric ulcers, there are other gastric lesions which require resection because they are precancerous. Gastric polyps are definitely premalignant lesions and should be treated by extirpation. Cromer and his associates[15], in a series of 195 cases of adenomatous polyps of the stomach, found that 35 (20 per cent) were malignant. In Marshall's series[16], 35 per cent of gastric polyps were associated with gastric carcinoma. There are certain cases of persistent atrophic gastritis in which gastric resection is desirable in order to prevent cancer. Konjetzny[17] believes that chronic gastritis is a precancerous

condition and that 85 per cent of gastric cancers develop on the basis of this lesion. A causal relationship between chronic gastritis and gastric cancer is considered likely also by Orator[18], Puchert[19], and Hurst[20]. Stout[21] is of the opinion that chronic gastritis must be regarded as a potential precancerous lesion.

Patients with pernicious anemia have a much higher incidence of cancer of the stomach than normal individuals. Rubin and Hodges[22] found the incidence of gastric cancer in pernicious anemia patients to be 10 times as high as in patients without pernicious anemia. At the University of Michigan Hospital[22], 2.5 per cent of pernicious anemia patients developed gastric cancer.

Cancer of the stomach should be diagnosed in a group of patients who previously were well but who have persistent gastric symptoms but in whom there is no evidence of a lesion of the stomach. This is particularly true of men, since gastric cancer is more frequent in men than in women, who beyond the age of 40 develop relatively vague gastric symptoms frequently consisting only of anorexia but persistent enough to cause a loss of weight of 10 or more pounds and in whom no lesion can be found either in the stomach or elsewhere to account for the symptoms. They are likely to have normal roentgenologic findings, normal gastric acidity, and the cytologic examination of the gastric contents is negative. Because of the possibility of a small gastric cancer producing the symptoms, it is imperative that these patients be explored to determine the presence or absence of a malignant lesion. We have had four such individuals with lesions so small that they could not be seen by any of the presently available methods of examination but in whom, at operation, a lesion a few millimeters in diameter was found. Radical subtotal gastrectomy was performed with, we believe, a cure in each instance. Had we waited until the lesion was demonstrable by the presently available diagnostic methods, there is a likelihood that the lesion would have become inoperable.

In the Ochsner Clinic from January 1, 1942 to January 1, 1954[8], 258 cases of primary gastric malignancy were observed of which 247 (95.7 per cent) were carcinoma, five (1.9 per cent) were leiomyosarcoma, three (1.2 per cent) reticulum cell sarcoma, and one each (0.4 per cent) Hodgkin's disease, lymphosarcoma, and neurofibroma. As mentioned previously, gastric cancer is primarily a disease of men. In our series of 247 cases[8], 169 (68.5 per cent) were men and 78 (31.5 per cent) were women. Gastric cancer, as in most cancers, occurs in older persons. The average age in our series in women was 59.9 years and in men, 57.8 years. Almost two-thirds of all the cases occurred between 50 and 70 years of age. In men, only 13.6 per cent of the gastric cancers occurred before 50 years of age, and 68 per cent occurred between 50 and 70; whereas, in women, approximately 17 per cent occurred before 50 years of age, and 54 per cent between 50 and 70 years of age.

The type of lesion varies according to whether it is considered from a clinical standpoint as determined by roentgenologic findings or by the patholo-

gist. In our series[8], most gastric cancers were diffuse. The roentgenologist diagnosed the lesion as being diffuse in 36.8 per cent, but the pathologist described the lesion as being diffuse in 65.6 per cent. Obviously, the latter is the more accurate description. The location of the lesion was determined clinically in addition to the diffuse involvement in 36.8 per cent and was as follows: pyloric, 13.8 per cent, in the cardia, 13.4 per cent, in the antrum, 11.3 per cent, on the lesser curvature, 9.7 per cent, in the fundus, 8.7 per cent, and on the greater curvature, 7.1 per cent. The pathologist, in addition to diagnosing 65.6 per cent as being diffuse lesions, 22.4 per cent were described as ulcerative, and 11.4 per cent as polypoid.

Clinical Picture

Almost without exception the early manifestations of gastric cancer are minimal and because they occur in older individuals who frequently have the misconception that as one grows older he should feel bad, the early symptoms are likely to be disregarded. We believe that in any person, particularly a man past 40, who previously has been well and free from any digestive symptoms and who develops for the first time anorexia or other digestive symptoms which persist in spite of therapy and which are sufficiently severe to cause a weight loss of 10 or more pounds, gastric cancer should be suspected. In our series of 247 cases of gastric carcinoma[8], there was an average duration of 8.7 months and an average weight loss of 25.7 pounds. Weight loss, in fact, was the most prominent manifestation of gastric cancer in our series, being present in 90 per cent. The symptoms in our 247 cases of gastric cancer at the time of admission were, in addition to weight loss, as follows: pain, 85 per cent, nausea, 58 per cent, tenderness, 55 per cent, anorexia, 52 per cent, simple vomiting, 47 per cent, palpable mass, 47 per cent, retention vomiting, 20 per cent, melena, 19 per cent, and dysphagia, 16 per cent. The physical examination in early cases of cancer is entirely negative and the presence of a palpable mass usually means extensive disease. This, however, does not preclude abdominal exploration, because occasionally a very large tumor which is locally invading but has not metastasized late is resectable and even curable. Fourteen years ago we saw a patient who had an enormous mass in the upper abdomen and x-ray evidence of carcinoma of the stomach, who was subjected to laparotomy. The lesion was an extensive carcinoma involving not only a considerable portion of the stomach but had extended by direct extension to the left lobe of the liver. An *en bloc* excision of the stomach, removing most of the stomach, the left lobe of the liver, the gastrohepatic, the gastrocolic and the greater omenta, and the regional lymph nodes was performed. This patient is well today after 14 years. This case, however, is the exception that proves the rule.

Diagnosis

As mentioned previously, it is a common concept that cancer of the stomach is readily diagnosed by x-ray, and although in our series of cases[8] a positive

diagnosis was made by the roentgenologist in 96.6 per cent, it is our firm belief that when a gastric lesion is diagnosable as cancer by x-ray, the lesion is far advanced and frequently inoperable. This is no reflection upon the roentgenologist because unless the lesion is large enough to produce an alteration of the gastric outline, it is impossible for the roentgenologist to suspect a malignant lesion. On the other hand, René Gutmann[23] of Paris is of the opinion that it is possible to make a diagnosis of gastric cancer relatively early. He believes that the lesion begins very slowly and persists for a long time before the classical growth which commonly is recognized as gastric cancer takes place. He also states that the incidence of malignant involvement varies in different parts of the stomach; that on the lesser curvature, the horizontal portion is the malignant area, whereas, the vertical portion of the stomach is the benign area. He emphasized the importance of examining the horizontal portion of the stomach with the patient lying down with stomach distended, and examining the vertical portion with the patient standing.

Because the results in the treatment of gastric cancer have been relatively poor, it is our conviction, as previously stated, that cancer of the stomach must be suspected long before the classical manifestations of a malignant gastric lesion are present, and it is only by suspecting gastric cancer earlier and by treating lesions which clinically are not cancer that the results will be improved.

Treatment

It is a well known fact that there is only one curative treatment in gastric cancer and that is the surgical extirpation of the entire malignant lesion. Unfortunately, there are a large number of patients with gastric cancer in whom the lesion is far advanced at the time the diagnosis is suspected. In our present series of 247 cases[8], 33 (13.4 per cent) were hopelessly inoperable when first seen. In a series of 11,737 collected cases[24], 78 per cent were operable and the operability incidence varied from 57 per cent to 90 per cent. Of our 214 patients with gastric cancer whom we considered operable, 16 (7 per cent) refused surgery, 198 were explored and 107 (54 per cent) were found to be nonresectable. Of the latter, 16 (15 per cent) died within the hospital. The resectability incidence in the 11,737 collected cases of gastric cancer was 42 per cent and the resectability incidence in the entire series varied from six to 63.3 per cent. Of our 198 cases which were explored, in 91 (46 per cent) a resection was possible. Of the 91 patients in whom a resection was done, in 60 (66 per cent) the lesion was advanced and extended beyond the stomach so that the procedure was considered a palliative one. Fifteen per cent of these died within the hospital. There were only 31 (34 per cent of all the resections) in whom the lesion had apparently not extended beyond the stomach. Of the 31 patients in whom the lesion was apparently limited to the stomach, 26 (83.3 per cent) had radical subtotal gastrectomies with a mortality rate of 7.7 per cent, four (13 per cent) had total gastrectomies with no deaths, and one (3.2 per cent)

had esophagogastrectomy with survival. Of the 31 patients in whom the lesion was apparently limited to the stomach only two (6.4 per cent) died as contrasted to the hospital mortality rate of 15 per cent when a palliative procedure was done and a similar mortality in a group of patients in whom no resection could be done but in whom some other type of procedure, either exploration or palliative procedure such as gastroenterostomy, was done. Obviously, the latter cases were much more advanced and the higher mortality rates in these cases was due to the disease rather than the operation. Of the 60 patients in whom the lesion had extended beyond the stomach but in whom a palliative resection was done, 39 (65 per cent) had subtotal gastrectomy, 13 (21.6 per cent) had total gastrectomy, and eight (13.2 per cent) had esophagogastrectomy. Of the entire 247 cases, 109 (44.1 per cent) had palliative operations, in 107 (43.3 per cent) the operation was not justified, refused, or had simple exploratory laparotomy, and there were only 31 (12.1 per cent) who had a so-called curative resection done.

End Results

Although obviously one is interested in the immediate survival of patients with malignant lesions, the ultimate survival rate is equally as important. In our 247 cases, 238 (96.3 per cent) have been actively followed. Of the nine patients lost to follow-up, none had any chance of cure because in none of them was gastric resection performed. The ultimate survival rate includes only those patients who survive and in no instance is exception made. Many of the patients who died following therapy, died of other conditions, but in each instance we have assumed that the patient died of the disease regardless of the cause of death. This is an extremely critical evaluation because approximately 15 per cent of the general population in this age group without cancer of the stomach are dead at the end of five years, but it is without bias because the personal equation has not entered into its determination. Of the group of patients in whom no resection was done because the lesion was far advanced, 22 per cent were alive at the end of six months, four per cent were alive at the end of one year, and 0.7 per cent were alive at the end of two years. No patient lived as long as three years. Of the patients in whom some type of resection was done, either palliative or curative procedures, 71 per cent were alive at the end of six months, 57 per cent at the end of one year, 46 per cent at the end of two years, 31 per cent at the end of three years, 26 per cent at the end of four years, and 21 per cent at the end of five years. Of the patients in whom a subtotal resection was done, whether it was done as a palliative procedure or as a curative one, 75 per cent were alive at the end of six months, 65 per cent at the end of one year, 53 per cent at the end of two years, 38 per cent at the end of three years, and 37 per cent at the end of five years. These statistics demonstrate that the results following radical subtotal resection are as good or even better than the results in all resections which include total gastrectomy as well as esophagogastrectomy. Obviously the results are best in a group of cases without obvious involvement

beyond the stomach. In a group of cases in which subtotal resection was done but in which there was no demonstrable nodal or other distant involvement, 81 per cent were alive at the end of six months, 80 per cent at the end of one year, 73 per cent at the end of two years, 69 per cent at the end of four years, and 57 per cent at the end of five years. On the other hand, of 37 patients in whom there was nodal involvement, 70 per cent were alive at the end of six months, 54 per cent at the end of one year, 40 per cent at the end of two years, 21 per cent at the end of three years, 17 per cent at the end of four years, and 12 per cent at the end of five years. These statistics demonstrate that if cancer of the stomach can be treated when there is no evidence of extension beyond the stomach the results are good, in that 57 per cent of those subjected to resection are well and free from disease at the end of five years. The results are even better than this, as previously stated, because many of the patients died of conditions other than cancer but all of them were considered as deaths from cancer. In the reported series[24], the five-year survival rates vary from 1 per cent[1] to 14 per cent[2,3]. The survival rate in the reported cases without lymph node involvement range from 26.9 per cent[25] to 56 per cent[12].

The survival rates varied considerably according to the type of lesion. The patient with diffuse lesion had the shortest survival rate. Of 155 with diffuse lesions, 29 per cent were alive at the end of six months, 13 per cent at the end of one year, 5.3 per cent at the end of two years, 2.4 per cent at the end of three years, and 1.8 per cent at the end of four years. No patient lived as long as five years. In 54 cases with ulcerative lesions, 70 per cent were alive at the end of six months, 62 per cent at the end of one year, 46 per cent at the end of two years, 36 per cent at the end of three years, 30 per cent at the end of four years, and 22 per cent at the end of five years. Of 27 patients with polypoid lesions, 48 per cent were alive at the end of six months, 36 per cent at the end of one year, 29 per cent at the end of two years, 17 per cent at the end of three years, 19 per cent at the end of four years, and 23 per cent at the end of five years. It is thus seen, as is to be expected, that diffusely infiltrative lesions offer a poor prognosis, whereas the prognosis in ulcerative and polypoid lesions is much better in that approximately one-fourth are alive at the end of five years.

Based upon our present experience, it may be stated that a group of cases of gastric cancer in which there has been an average delay of 8.4 months from the first symptoms until definitive therapy is instituted and in which the lesion is diagnosable as gastric cancer in almost 97 per cent of cases, the results are not good. Eighty per cent were explored, 37 per cent were resectable, 32.4 per cent survived resection, and only 7.2 per cent are alive and apparently well at the end of five years. These results are indeed far from the ideal. As previously indicated, it is essential that something must be done to alter the pessimistic outlook in a patient with a malignant lesion of the stomach. It is our belief that the results can be improved, but they can be improved only in one way and that is, earlier diagnosis. If physicians continue to wait until an individual

with a gastric complaint shows unmistakable evidence of gastric cancer before this lesion is suspected and before therapy is instituted the results are going to continue to be bad. Only by the treatment of lesions which clinically are not cancer and by suspecting gastric cancer in men past 40 who previously were free from digestive symptoms but develop symptoms severe enough to cause a weight loss of 10 or more pounds in spite of therapy, can the results be improved in gastric cancer. We are convinced that all gastric ulcers should be treated by resection, not only because it is impossible to differentiate between benign and malignant ulcerative lesions of the stomach, but also because the results following gastric resection are better than the results obtained by conservative therapy. It must be emphasized that this statement is made concerning gastric ulcers and not duodenal ulcers. We are of the conviction that duodenal ulcers are primarily medical lesions and should be treated conservatively, and only when a surgical complication exists or in the rare case in which the lesion is intractable should surgical therapy be instituted. The results, however, following surgical treatment of duodenal ulcer are not as good as results obtained following the surgical treatment of gastric ulcer. Because of the impossibility of differentiating benign and malignant ulcerative lesions and also because we believe that benign gastric ulcers can and do become malignant, the physician who undertakes conservative treatment of a gastric ulcer assumes a tremendous responsibility.

In addition to gastric ulcers, all gastric polypi should be removed. Many patients with persistent chronic gastritis should have the advantage of gastric resection because chronic atrophic gastritis is in many instances a premalignant lesion. Persistence of gastritis in pernicious anemia should be followed with considerable caution and many of these patients should have the advantage of gastric resection. Abdominal exploration is obligatory also in the relatively rare instance of gastric distress, in a man past 40 who was previously well, which persists and causes weight loss of 10 or more pounds in spite of therapy, but in whom x-ray examination is negative, gastroscopic examination is negative, and even in whom there may be normal gastric acidity. Occasionally such an individual will have an early cancer which is diagnosable only by abdominal exploration and if one waits until the lesion is diagnosable as cancer, it is likely to be so far advanced that cure is not possible. If one adopts this philosophy, undoubtedly there will be an occasional patient operated upon unnecessarily and although I would be the last to condone an unnecessary operation, I believe that it is better to do an occasional unnecessary laparotomy than to allow an operable gastric cancer to become inoperable until the lesion can be proved preoperatively.

Conclusions

1. Gastric cancer has been, since the time of the ancients, a common cancer and the results from its treatment today are little, if any, better than 25 years ago.

2. Although a radical cancer operation is necessary in order to treat all cancer, total gastrectomy is not necessary in most cancers of the stomach. Equally as good results can be obtained by a radical subtotal resection of the stomach with an *en bloc* excision of the omenta and regional lymph nodes in cases of cancer of the stomach not of the infiltrative type or those limited to the proximal half of the stomach.

3. Results in gastric cancer will be improved only by earlier diagnosis and institution of curative therapy at a time while the lesion is still limited to the stomach. If the diagnosis is delayed until the lesion can be diagnosed clinically as cancer, frequently the case is hopeless.

4. Lesions which are not clinically cancer should be treated as if they were cancer. All gastric ulcers should be resected. Gastric polypi and many cases of chronic gastritis should have a gastric resection.

5. Men past the age of 40 who have persistent gastric symptoms causing weight loss in spite of therapy should have the advantage of an abdominal exploration.

6. The results following the radical subtotal resection are good if the lesion can be treated while it is limited to the stomach. One-half to two-thirds of such patients are alive and well at the end of five years.

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Discussion

Dr. I. Snapper:—Everybody will agree with Dr. Ochsner that it is necessary to diagnose carcinoma of the stomach in a very early stage. Unfortunately patients harbor carcinoma of the stomach for a considerable time before they have complaints. I have seen two examples where during a cholecystectomy for gallstones, palpation of the stomach revealed the presence of a small carcinoma. In both cases the surgeon did not feel justified to perform a total resection of the stomach without special authorization. Both patients did not wish to be operated again because they felt perfect after having been liberated from their gallstones.

Both patients went on for two years, without any complaints, without any loss of weight. The first complaints of the stomach started only after two years. It seems well nigh impossible to diagnose patients with gastric carcinoma in the early stages of the disease if the tumor can grow for at least two years before the first clinical symptoms and signs develop.

Difficulties will be encountered if every middle-aged person who loses weight would be subjected to an exploratory laparotomy. In our country it is correctly emphasized that no treatment should be started unless a diagnosis is established. This is the reason why the tissue committees which guard the standards of surgical practice in most American hospitals look askance at exploratory laparotomies.

Dr. Ochsner's recommendations might well lead to a revival of the practice of exploratory laparotomies. Most surgeons who would perform a series of such operations without finding stomach cancer would encounter severe criticism by tissue committees.

Dr. Harry A. Oberhelman:—Now, as far as carcinoma of the stomach is concerned, I do want to compliment Dr. Ochsner on his statistics, although Dr.

Snapper didn't seem to feel that way, but so often we see statistics that include only those cases that have given us the best results. Those that could be excluded he has included, and has given to me, at least, a really fine, honest presentation of statistics.

It has been my impression that our survival rate of five years or more is considerably higher than it was 15 or 20 years ago. I know that at that time we had a survival rate of almost zero. Then it did approach the figure of 2 or 3 per cent, and then it reached the figure that was quite commendable, 5 per cent of five-year survivals. In my experience, it has run a little bit higher than that. I am not sure whether it is all on the basis of radical resection or not.

I have two women now that have gone eight years following gastric resection for carcinoma. It was not even a radical subtotal, as Dr. Ochsner pointed out, and those two women are still alive. I did not search high for the glands, nor did I remove the omentum in those cases. They are still living.

When we see such situations, we get a little confused as to what we might attribute an increased survival rate in cancers of the stomach. I do feel that earlier diagnosis, of course, is indeed the most basic principle and, if we can get early diagnosis, we have a much better chance.

I do want to say that many times, in our experience with our roentgenologists, the lesion is much larger in the x-ray than we find at surgery, or vice versa. When it is the other way around, you are confronted with a problem you had not anticipated.

I did not want to leave a wrong impression about ulcers of the stomach. I am not backtracking by any means. I do feel that, when we recommend gastric resection for our patients with gastric ulcer, I am speaking of people under 40—Dr. Ochsner, I don't believe, mentioned an age limit there; I don't know whether he advocates radical surgery or subtotal resection for young people in the 20's, with gastric ulcer. In people of 40 years or over, I feel that, if there is a dramatic response to conservative management, and in the x-ray the ulcer has entirely disappeared, we can go along with such a patient for some time, maybe indefinitely, maybe for the rest of his life.

I say that because that might be my ulcer and, if it is my ulcer, I will probably want to treat it that way. So, those are some of the other aspects.

Also, when you are doing gastric surgery for these ulcers and you have had some bad results, maybe you have gotten a stomal ulcer in a series of your resected cases for gastric ulcer. You stop, look and listen, and resurvey the field. I do think that every case in itself is individual.

Dr. Ochsner gave a very marvelous presentation of the subject, and I am impressed with his enthusiasm; I think his words are well taken. It is very true that no one can tell whether the lesion is carcinoma or not until the pathologist looks at it.

A few years ago I attended a morning session at the Massachusetts General Hospital put on by Arthur Allen and his group covering a gastrointestinal surgery over a ten-year period. I was very much impressed by it. One of the jewels that I gathered from that discussion was this fact: In their series of gastric ulcers, 10 per cent that were considered benign by the clinician, as Dr. Ochsner pointed out, by the roentgenologist and, I hesitate to say, by the operating surgeon who should be able to tell, proved to be malignant. So that in 10 per cent of the gastric ulcers that were resected, that were thought to be benign by the clinician, by the roentgenologist, by the surgeon and, grossly, by the pathologist, but microscopic section proved otherwise. So, I would like to leave it more or less as an open matter. I think each case is individual.

Dr. Alton Ochsner:—I knew this was going to provoke a great deal of discussion. I am not astounded by it nor am I disappointed; I am very pleased.

I was tremendously impressed by Dr. Snapper's discussion, and it pleased me very much to think that an internist would have been so much impressed by the policy of the American College of Surgeons. That pleases me very much. I would be the first person to condemn an unnecessary operative procedure. There is no question that, if one adopts this philosophy, there will be an occasional laparotomy which will not prove fruitful, as far as finding the lesion is concerned. On the other hand, I would have no objection, to telling the patient that I was wrong and he did not have cancer. Up to the present time, however, I have not operated upon one of these people unnecessarily. So far I have always found the lesion, but the time is coming when I will not.

I would have no hesitancy in coming before the Tissue Committee, to explain why the laparotomy was done and the lesion not found. You have no difficulty in justifying that stand, because we are interested in controlling or curing a disease which has pretty much defied treatment up to the present time.

I admit that this philosophy is a revolutionary one. We are dealing with a relentless enemy. Unless we change our tactics, our results are going to be just as bad as they have been up to the present time.

If I opened up an abdomen and did not find evidence of a neoplasm, I would not do a resection. Some of my friends have asked me whether I would think one would be justified in doing a resection on symptoms only. No, I do not. I think one would have to have evidence of it. I feel the same way about the gastric ulcer.

Dr. Oberhelman said if he had a gastric ulcer, he would not subject himself to operation. Of course, that is his privilege to decide what he wants and what he doesn't want. I can assure you, however, that if I had a gastric ulcer, I would be operated upon.

It has been brought out by both discussers this morning that there are some cancers of the stomach that are very invasive from the very beginning,

and even though they are operated upon early and picked up accidentally, they can't be cured. There is a great variation in the natural history of many of these diseases.

On the other hand, in the majority of them, if they could be treated relatively early, the results would be much better. That is the thing I am trying to get over to you. This is not a hopeless problem at all. It is a problem in which the results can be improved, but only by everyone being cognizant of it and trying to institute therapy at the time when something can be accomplished.

I would take exception to Dr. Snapper's statement that a gastrectomy is a dangerous operation. I don't think it is a dangerous operation at all. I think cancer of the stomach is dangerous. A gastrectomy is not desirable. I wouldn't want to have a gastrectomy either, unless it was necessary, but if there were any question about my having a gastric cancer or an ulcer that might be cancer, I would certainly take the lesser of the two evils, which would be gastrectomy.

Again, I would have no objection to any one of you saying, "I don't want to have my stomach taken out simply because I have an ulcer." You may not want to. I think if you assume the responsibility of letting your own ulcer be treated conservatively or letting your patient's ulcer be treated conservatively, you are assuming a responsibility that I don't think is justified.

Dr. Oberhelman asked me if I advised resection in young people. One might reason, "Well, the young person is less likely to have gastric cancer." I am perfectly willing to admit that, yet I am not convinced that a scar persisting on the epithelial surface which is so likely to undergo malignant change as is the gastric mucosa may ultimately lead to gastric cancer. I admit I am treading on dangerous ground here because the concept today among pathologists is that most gastric ulcers do not become malignant, in contradistinction to what it was 30 years ago.

Stout, in New York, on the other hand, believes that gastric ulcers are premalignant lesions. I don't know whether they are or not. I think you can take your choice.

Dr. Oberhelman referred to the difficulty in interpreting the results because two patients who had advanced lesions, in whom he didn't do radical procedures got well. That simply shows there are some patients with advanced lesions who have a slowly growing tumor and still can be cured. That doesn't mean that we shouldn't be on the lookout for these early cases because, by the diagnosis of the early cases, we are going to accomplish a great deal more.

I would be interested to learn from Dr. Oberhelman whether he has observed stomal ulcer following gastrectomy for gastric ulcer.

Dr. Oberhelman:—One or two.

Dr. Ochsner:—It is so rare following gastric ulcer that one can almost disregard it. It is not rare following duodenal ulcer.

The results following the surgical treatment for gastric ulcer are so good, so much better than the results following surgical treatment of duodenal ulcer, they can't be compared.

Again I say that those of you who do not want to subject your patients or have your patients subjected to a gastrectomy for gastric ulcer, should at least have the ulcer removed and subjected to careful serial sectioning to determine whether it is cancerous. I, however, do the radical subtotal resection in all patients with large gastric ulcer.

We had three patients within the period of about nine months who had what I thought were benign ulcers, and I did a subtotal resection. We got frozen sections at the time of operation, and they were benign. We did not take out the lymph nodes and did not take out the omentum or as much stomach. When the final section came through, all three were malignant. I had to go back and do the radical procedure.

Although in those cases in which the lesions were not malignant, the patient has been subjected to an exceptionally radical procedure, actually their results are good. I think it is better than running the risk of having to go back, although I would have no qualms or no objection to one who wanted to do a less radical procedure for the case which has not been proved to have cancer.

I sincerely hope that I have stimulated enough interest in you to make you suspect cancer and make you a little more conscious of your obligation when you advise conservative treatment of these lesions which might be mimicking cancer.

If you are willing to assume that you can differentiate between a malignant and benign ulcer, which I don't think anyone should be willing to assume, then that is your responsibility. I am sure it is only by adopting a philosophy such as this that we are going to improve the results. The results now are bad. Although Dr. Oberhelman said it was his impression the results are better, unless you have recently gone over your cases, I am afraid your impression is going to be like my impression was. As I always tell our house staff and our own staff, when I have an impression about something, it is likely to be wrong because I remember the good results and I forget the bad results. It is only when you sit down and go over all your cases that you really know what is happening.

These statistics I gave this morning are based upon the reports from the better institutions in the United States. This is a résumé or summary, a collection of all the cases in the United States reported for about the last 15 years. The five-year survival rate in that group is 5 per cent.

THE DIAGNOSIS AND TREATMENT OF POLYPS OF THE RECTUM AND COLON*

ROBERT T. McCARTY, M.D., F.A.C.G.†

Milwaukee, Wisc.

Polypoid disease of the rectum and colon has received much attention in the past three decades. In the gastrointestinal tract, carcinoma of the rectum and colon is second to the stomach in frequency, and fourth most common in the body.

Woodward[1], in 1881, was the first to differentiate the true polyp from the pseudopolyp of inflammatory disease.

Investigators interested in this disease have thrown much light on the distribution of polyps in the colon and rectum, the importance of the benign polyp, familial polyposis coli and the relation of the benign polyp to carcinoma.

Woodward, Dukes, Helwig, Frankfeldt, Buie, Swinton, Bacon and many others, have done much to stimulate our interest in this disease. They have emphasized the importance of the polyp in preventing carcinoma.

An adenomatous polyp of the rectum and colon may be defined as a proliferation of the structure of the glands of Lieberkühn which produces sessile or pedunculated growths.

Polyps may begin as benign or malignant growths, according to Helwig[2]. All benign polyps are potentially malignant.

Hennessy[3] found that 30 per cent of cancers of the rectum and colon are a result of malignant degeneration of a benign polyp. We have observed two case of benign polyps transforming into malignant polyps in 12 months.

Helwig[2] states that one person in five may develop one or more polyps. This demonstrates the frequency of the disease. Multiple polyps are frequently found, the figures varying from 15 to 25 per cent in those having the disease.

Burnikel and Schutte[4] have shown that in 5,072 sigmoidoscopic examinations, 500 had polyps, an incidence of 9.5 per cent. This did not include those found in colon x-rays. The Wisconsin State Board of Health reports that 950 persons die each year of cancer of the rectum and colon. Burnikel and Schutte[4] further show that 74.4 per cent were solitary and 15.6 per cent were multiple. Though they are more frequent after 40, they may be found at all ages. I recently saw an 11-month old child with multiple polyps scattered from the

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†Associate Professor of Surgery, Marquette University School of Medicine.

cecum to the anus. Kerr has shown that they are one of the more common causes of bleeding in children.

The distribution of polyps according to Boehme[5], is as follows: cecum 6 per cent, ascending colon 3 per cent, hepatic flexure 3 per cent, transverse colon 4 per cent, splenic flexure 2 per cent, descending colon 4 per cent, sigmoid 12 per cent, rectum 53 per cent and anus 0.6 per cent. About 15 per cent are in the right colon and 85 per cent in the left colon and rectum.

A simple classification is as follows:

A. Adenomas

1. Pedunculated — Single / Multiple
2. Sessile — Single / Multiple
3. Familial multiple polyposis coli.

B. Villous papilloma

C. Polypoid vegetations or psuedopolyps.

Histogenesis

Dukes[6] believes that the villous papilloma is derived from the mucosal surface epithelium, whereas an adenoma is derived from the glands of Lieberkühn.

In 1952 Swinton and Doane[7] reviewed 300 cases of benign polyps of the colon and rectum and found 20 or 6.6 per cent to be villous papillomas.

Sunderland and Binkley[8] found 68.7 per cent of papillary adenomas showed areas of cytological carcinoma.

Diagnosis

One cannot overemphasize the importance of a careful history. Rectal bleeding, change in bowel habit, diarrhea, constipation, protrusion from the anus, or unexplained hypochromic anemia, are the most common symptoms. Infrequently, bowel obstruction due to intussusception is seen. Let us not underestimate bleeding, regardless of how slight. Let us keep in mind that one may have a rectal problem such as hemorrhoids, and a polyp of carcinoma at a higher level.

The most common symptom of a villous papilloma is bleeding. Next is diarrhea, and excretion of large amounts of mucus. The diarrhea is usually more severe in the morning.

The examination should include inspection, digital examination (and as the finger is removed from the anus, look for the presence of blood), anoscopic and sigmoidoscopic to the 25 cm. level or higher if possible. The polyp can be seen as it is intrinsic. Carefully look behind the rectal valves and folds of mucosa. The presence of a streak of blood with mucus indicates a lesion at a higher level when seen through the inserted sigmoidoscope.

Small polyps cannot be felt but can be seen. The villous papilloma feels soft. It is usually located in the rectum. A firm part indicates malignant degeneration. Remember that the 25 cm. sigmoidoscope covers the area where 70 per cent of the lesions are found.

The colon x-ray and contrast air study should only be done after the sigmoidoscopic examination. The x-ray can only be held responsible for 30 per cent of the lesions, and only when they are 0.5 cm. or larger. The x-ray without the sigmoidoscopic examination only gives a false sense of security when negative.

About 50 per cent of the polyps are "silent", as they are too small to give symptoms. Therefore, it is strongly recommended that the proctosigmoidoscopic examination be made a part of a general physical examination. This point is being emphasized in our training of medical students and residents. When a polyp is found, a careful study should be made as to classification, consistency, size, color, bleeding or not bleeding, ulcerated, smooth, nodular, movable or fixed.

When a polyp is found, a decision must be made on treatment and all polyps should be biopsied, regardless of size.

The small pedunculated polyp can be removed with electric snare and the base fulgurated. The sessile polyp can be removed with a biopsy forceps. If small, an excision biopsy should be done and the base should be fulgurated. If large, a biopsy should be taken at its edge to get mucosal cells as well as tumor cells. As much of the tumor as possible should be sent to the pathologist with a complete description as to site and clinical pathology. The exact location must be noted and recorded with complete description as previously indicated.

Treatment

The biopsy report will help decide on the treatment.

A complete removal and fulguration of the base of the benign polyp is adequate. Malignant change at the periphery without the invasion of the stalk in the pedunculated polyp or *muscularis mucosae* in the sessile polyp is adequate treatment, in the opinion of Castleman[9]. If malignant and there is invasion of the pedicle or *muscularis mucosae* and the location is below the rectosigmoid,

an abdominoperineal resection is indicated. If in the sigmoid or higher, an anterior resection is indicated. This is the treatment advocated by Fisher and Turnbull[10].

The villous papilloma, when possible, should be excised *in toto*. It is a tumor which is usually located in the rectum and is amenable to this procedure. If malignant, radical surgery as abdominoperineal resection is indicated.

Summary

1. Polyps of the rectum and colon may be benign or malignant.

2. The benign polyp is potentially malignant.

3. About 70 per cent of the polyps are within reach of the 25 cm. sigmoidoscope. Therefore the sigmoidoscopic examination should be a part of a general physical examination.

4. All polyps should be biopsied or removed *in toto* for pathological evaluation.

5. A proctosigmoidoscopic examination should precede a colon x-ray.

6. If benign, complete removal of the polyp is adequate; if malignant, radical surgery is indicated.

7. All polyp cases should be followed at regular intervals for at least 5 years.

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Discussion

Dr. Harry A. Oberhelman:—This last paper I think was outstanding. I am not going to say much, if anything, about this because it was complete, and I

am sure there is nothing more I could add. I had one question in mind, and Dr. McCarty very graciously answered that. It was what shall we do with these polyps that have a long pedicle and are, on the surface, malignant. He answered that for me. He says they may be removed locally. That has been my experience with these lesions.

Dr. I Snapper:—Dr. McCarty emphasized the very important point that large amounts of mucus may indicate the presence of villous adenoma of the sigmoid.

NUTRITION AND GASTROINTESTINAL DISEASE*

SEYMOUR L. HALPERN, M.D., F.A.C.G.

New York, N. Y.

The intent of this review is to correlate and systematize some of our current knowledge concerning nutrition and gastrointestinal disease. This knowledge derived from recent nutrition and metabolic studies is not yet being utilized sufficiently by many physicians.

It has been found that the correct application of the principles of nutrition therapy will facilitate the treatment of diseases of the gastrointestinal tract and avoid the injurious effects and prolongation of convalescence that result from improper diet therapy. By applying reasonable judgment, perspicacity and circumspection when formulating diets, one can prevent iatrogenic disorders consequent to a contumelious attitude toward nutritional therapy born from familiarity with food and nutrition.

Nutrition admittedly is the most important environmental factor which influences the overall state of health and disease. No closer relationship exists than that between nutrition and the gastrointestinal tract. Under normal circumstances, the nutrition of the entire body enters via this system. There the foodstuffs ingested are converted into a form which is available to the metabolic machinery of the body's cells. A healthy, normally functioning gastrointestinal tract that permits proper digestion and absorption of foods is a prerequisite for the most efficient utilization of dietary nutrients and thus for the optimal state of nutrition and metabolism of all organ systems. On the other hand, the tissues of the gastrointestinal tract are not immune to the influences of metabolic alterations consequent to a varying dietary pattern. When there is a failure to maintain the most favorable state of nutrition, they will be affected adversely in a manner similar to the other major organs of the body.

A Dangerous Vicious Cycle

The above facts establish the basis of one of the most frequent and important vicious cycles seen in medical practice. Many organic and emotional disturbances, in addition to primary gastrointestinal disease, cause anorexia, "indigestion", flatulence, impaired enzyme secretion, defective absorption and disturbed gastrointestinal motility—all abnormalities which interfere with the intake, digestion and absorption of essential nutrient elements. A conditioned caloric, protein, vitamin, and mineral malnutrition may be a consequence. Among the manifestations of the generalized deterioration of the tissues pro-

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duced by this state of malnutrition are further diminution of appetite, loss of weight, decreased gastric and intestinal secretions, either chronic diarrhea or diminished motility within the intestinal tract, reduced absorptive capacity of the small bowel, and impaired hepatic and pancreatic function. A noninflammatory degeneration of the mucous membranes of the intestinal tract may be produced and changes in liver cell morphology are common.

Functional disturbances may be revealed by a flat oral glucose tolerance test, analysis of fat, muscle and enzyme content of the feces, gastric analysis and similar studies. Roentgenographic and sigmoidoscopic examinations may demonstrate anatomical changes. Such disturbances within the gastrointestinal tract, of course, have in themselves the capability of leading to a state of nutritional deficiency. Insufficient attention to, rather than lack of awareness of, the potential vicious cycle of: gastrointestinal disease → malnutrition → accentuated gastrointestinal dysfunction → increased malnutrition, has resulted in numerous therapeutic failures in medical practice.

It is not unusual to see patients with gastrointestinal disease in whom it almost is impossible to delineate which of the symptoms and signs are attributable to a primary disorder of that organ system and which are secondary to a nutritional deficiency. All too frequently, symptoms and signs that in actuality are manifestations of a deficiency disease are attributed to some other obvious abnormality. Failure to recognize the true etiological mechanism in such cases may lead to unwise further dietary regimentation with perpetuation of the physiological and pathological disturbances. Only meticulous attention to the total nutrition of the patient, while concomitant specific and supportive therapy is being rendered for primary and secondary gastrointestinal symptoms and organic disease, can break the vicious cycle with its consequent obstruction both to total therapeutic success and to rapid convalescence from disease.

Special Problems of Nutrition in Gastroenterology

Many aspects of the subject of nutrition and gastrointestinal disease require elucidation. These include:

1. The role of nutritional deficiencies, primary and/or conditioned, in the pathogenesis of gastrointestinal illness. For example, an inadequate supply of folic acid, Vitamin B_{12}, animal protein and Vitamin B-complex in the diet can lead to the sprue syndrome.

2. The role of gastrointestinal dysfunction in the etiology of malnutrition. In chronic ulcerative colitis, as we all know, protein disequilibrium, with all its serious implications, is common.

3. The frequency with which diet therapy itself produces overt and subclinical "iatrogenic" malnutrition. The diet regimen for peptic ulcer and, in fact, many other therapeutic diets as outlined in medical textbooks and hospital

dietary manuals, frequently are lacking in total nutritional adequacy, especially in the protein and vitamin requirements.

4. Diagnostic methods by which we can increase our ability to distinguish primary from secondary disturbances. It is of vital importance, for instance, to determine whether a severe failure of appetite is due to a primary organic disease, whether it is a selfperpetuating anorexia consequent to a poorly conceived therapeutic diet or whether the lack of desire for food is a symptom of emotional and psychic upsets.

5. The therapeutic nutrition of gastrointestinal disease. In acute infections, chronic arthritis, cardiovascular disease and certain other disorders specific therapy may have the primary therapeutic role although diet therapy is an essential adjuvant to insure successful treatment, to prevent side-effects from pharmacological agents, to decrease the duration of convalescence and, in general, to increase cellular resistance. Contrariwise, in treating diseases of the stomach, small intestine, colon, liver, gallbladder and pancreas, the nutrition regimen commonly is the principal basis of treatment. In these disorders pharmaceutical preparations are the therapeutic adjuvants.

The subject of "therapeutic nutrition of gastrointestinal disease" properly should be subdivided into:

a. specific diet therapy directed at alleviating the gastrointestinal pathology and dysfunction; and

b. nonspecific therapeutic nutrition concerned with the prevention and treatment of nutritional deficiencies.

6. Psychological aspects of therapeutic nutrition. The diet regimen imposed upon the patient too frequently is more productive of physical, social and emotional invalidism than the initial disease process itself.

In the brief time allotted to me it obviously is impossible to discuss in detail any of the aforementioned phases of nutrition and gastroenterology. My observations during the remainder of this paper, therefore, will be confined to some special problems and practical aspects of the therapeutic nutrition of gastrointestinal diseases.

Total Adequacy of the Diet

The major problem in all nutritional programs is to insure total adequacy of the diet. The attention of the physician who is outlining a patient's diet never should be so closely focalized on the disease process that the total adequacy of the diet is inadvertently overlooked. Good nutrition, when present, must be maintained and the development of deficiencies must be prevented. Poor nutritional states should be corrected as quickly as practicable.

When composing a diet, therefore, cognizance must be taken of the daily needs of the patient, previous nutritional depletion and current losses. The normal as well as the special nutritional requirements must be accounted for. The quantitative composition of the diet cannot be determined solely from the recommended allowances for healthy people. One must appraise also the additional demands that the illness makes for specific nutrients. The caloric content of the diet, for example, will be determined by adding to the estimated number of calories required by the total daily energy expenditure of the patient, the amount of calories lost from the system, as by diarrhea or vomiting, and the quantity needed to compensate for any previous weight loss as well as the current status of overweight or underweight. The diet program also must take into account imbalances in the interrelationships between nutrients, interferences with utilization of specific nutrient elements and the catabolic loss of nitrogen, vitamins and minerals which may be produced by the disease process. If feasible, all the essential nutrient elements should be supplied to the tissues simultaneously in the appropriate quantities and proportions.

Failure to insure total diet adequacy may induce a malnutrition that can cause tissue healing to be delayed and convalescence to be prolonged. Unfortunately, this prolongation of the duration of an illness that results from dietary inadequacies only infrequently is ascribed to its actual cause.

Diarrheal Diseases

In severe diarrheal states food may not be retained in the intestinal tract for a sufficient length of time to permit its absorption. Conspicuous malnutrition and metabolic disturbances may result from superimposing a starvation effect produced by this absorptive failure upon serious losses of fluid, electrolytes, other nutrients and perhaps blood. Dehydration, acidosis, renal failure, starvation ketosis, hepatic damage and hypochromic anemia may occur and complicate therapy.

In acute diarrheal states it may be necessary to place the gastrointestinal tract at rest for a period of time which will be determined by the nature and severity of the disease. Parenteral alimentation frequently becomes indicated. When oral therapy is feasible, this is preferable. A bland, low-residue diet is administered. It should be served frequently and in small amounts. These diets must be high in proteins, with a minimum of 1.5 to 2 gm./kg./day, and high in calories. Protein concentrates, such as dry skim milk powder, can be utilized to achieve necessary protein levels. Suitable unsweetened carbohydrates, such as lactose, and emulsified fats may be added to the diet where a high caloric level otherwise cannot be achieved. Vitamin supplements should be added to the diets of all such patients.

When parenteral alimentation becomes necessary, sufficient fluid must be given both to supply the daily needs for maintenance and to compensate for

losses through the bowels. Losses of sodium, chloride and potassium should be corrected early by appropriate solutions. Since isotonic sodium chloride contains an excess of chloride over sodium compared to their concentrations in the blood, 1/6 molar sodium lactate solution may be substituted for isotonic sodium chloride when acidosis is present or imminent. At least 100 gm. of glucose should be administered daily. This will conserve tissue protein and prevent ketosis. Protein hydrolysates are required only if parenteral alimentation must be continued for more than 48 hours. Ten per cent dextrose or levulose solutions should be used in an attempt to increase total calories. Even so, caloric needs rarely are fulfilled during periods of parenteral alimentation. Solutions of water-soluble vitamins should be added to the infusions. It is advisable to resume oral feedings as soon as possible.

In ulcerative colitis and other chronic diarrheal diseases bland, low-residue diets are indicated for prolonged periods of time. It may be necessary to provide a diet containing 150 gm. of protein and 4,000 calories daily in order to prevent tissue protein depletion and loss of body weight. Such high protein diets may be required for several months to correct protein deficits.

In chronic ulcerative colitis, the ability of the physician to induce the patient to consume a very high protein, high calorie and high vitamin diet frequently is the determining factor in successfully effectuating a clinical remission. One of the principal reasons that ACTH, cortisone and related compounds have a beneficial effect in accelerating recovery is that they cause food intake to be increased by improving the appetite, while minimizing nutrient losses through decreasing the diarrhea. The use of frequent, small, concentrated, nutritious liquid feedings at times is helpful. Tube feeding occasionally is required. Transfusions are valuable only if a severe anemia is present. Supplemental vitamins are necessary and may be given parenterally to insure their effective utilization.

Stomach Diseases

Bland diets are indicated for gastritis of any etiology. Nutritional depletion occurs when there is protracted vomiting because of complete lack of intake with superimposed losses. The loss of hydrochloric acid can result in alkalosis. On the other hand, the starvation effect may produce an accompanying ketosis. It may become practicable to withhold oral feedings and to give parenteral alimentation for 2 to 3 days. The excess of chlorides present in isotonic saline will be of assistance in replacing chloride losses.

The traditional Sippy-type diets used in the treatment of peptic ulcer are inadequate in proteins and also in calories. It is conceivable that the tissue hypoproteinemia which can occur may actually interfere with the healing of the ulcer. Patients who have a peptic ulcer should receive a minimum of 70 to 100 gm. of protein per day in the diet. The addition of milk powder and other

oral whole protein preparations will help to achieve protein and caloric balance and, by their own buffer action, add to the acid neutralizing effect of cream-milk mixtures.

Liver Diseases

A high protein, high calorie, high vitamin diet remains today the most effective treatment for liver diseases. In both acute and chronic hepatic disease the diets administered should contain about 1.0 to 1.5 gm. of protein per kg. of body weight and approximately 3,000 calories. With sufficient protein and carbohydrate in the food plan, the low fat diets once recommended for cirrhosis and hepatitis become unnecessary. When bile is present in the intestinal tract, as much as 100 gm. of fat may be given daily. This fat will simplify the caloric problem, make the diet more appetizing and easier to prepare, and may supply certain essential unsaturated fatty acids to the body.

Vitamin supplements should be given to all patients with hepatic disease. Brewer's yeast is helpful. Lipotropic substances such as choline and methionine cause questionable benefits when the diet contains sufficient protein and is otherwise adequate. Intravenous liver extracts and human serum albumin preparations are of no additional value. Alcohol and hepatotoxins are interdicted.

When cirrhosis of the liver is associated with ascites and edema, sodium must be markedly restricted since patients in this decompensated state excrete only small amounts of sodium in the urine regardless of the quantity of salt administered. Mercurial diuretics, carbonic anhydrase inhibitors, and ion exchange resins, all of which cause a loss of sodium from the body, are helpful in the treatment of patients with ascites and/or edema.

Nutritional Gastrointestinal Disorders

It is essential to recognize early those gastrointestinal disturbances which arise as a result of nutritional deficiencies. In these cases specific therapy can be administered readily and a relatively prompt clinical response may be anticipated. Lesions which result from nutritional disturbances usually are reversible even in their late stages. In rare instances, a state of "malignant malnutrition" may develop. This is characterized by extreme fat infiltration in the liver and other irreversible changes are found. It commonly has a fatal outcome.

The diarrheas of sprue and pellagra as well as other bowel disturbances that result from nutritional inadequacy are ameliorated rapidly following the institution of replacement therapy. It is noteworthy that even the marked functional and anatomic derangements of the liver and pancreas which are seen in kwashiorkor regress when the previous malnutrition is corrected by administering a diet high in animal proteins.

Many nonspecific gastrointestinal symptoms and physiological disturbances are relieved by ingesting diets high in vitamins, especially of the B-complex, and high in animal proteins. Whenever gastrointestinal disorders not due to an obvious cause are seen in individuals whose diet history or physical examination gives evidence of single or multiple nutritional deficiencies, an abundant diet with a high content of essential nutrients should be given a therapeutic trial. Remarkable cures occasionally are the reward.

Rare is the disease for which it is impossible to fashion a diet that contains adequate quantities of calories, proteins, vitamins and minerals. When there is evidence of previous depletion, or when there is any question concerning the total adequacy of the diet, it is advisable to administer dietary supplements. Excellent maintenance and therapeutic vitamin preparations are available for this purpose. Extra protein may be given, as noted, in the form of eggnogs or by adding to the food dried skimmed milk or other whole protein preparation or perhaps even, in certain instances, protein hydrolysates. If one cannot administer successfully additional calories in the form of eggnogs or other nutritious drinks, special caloric concentrates, such as Lipomul and Ediol, may be utilized. It is as inexcusable to permit signs of a nutrient deficiency to persist without immediate attempts at correction as it is for a patient who is under medical surveillance to develop symptoms or signs of a dietary inadequacy.

Anorexia

Anorexia frequently presents a major obstacle in the pathway to successful nutritional therapy. This symptom accompanies the majority of gastrointestinal disorders. Vigorous endeavors must be made to induce the patient to eat. It frequently is enough to explain to the patient that he has entered a vicious cycle from which he may escape only by ingesting more and better food. As nutrition improves, the appetite usually will improve and a favorable cycle of events will be initiated. Appetite training may be a tedious process. It is necessary to cater to the patient's idiosyncracies, while preparing appetizing menus. Food habits, likes and dislikes must be taken into consideration. Time spent in this fashion will obviate the need to resort to cortisone, testosterone, insulin and other endocrine agents. These have been used with irregular results and present the danger of harmful side-effects.

The severely anorexic patient often will tolerate liquid feedings. It is not difficult to prepare nutritious liquid mixtures that will supply to the patient all his requirements for proteins, calories, vitamins and minerals. Recently, several commercial preparations, such as Sustagen, have been developed which facilitate the preparation of liquid mixtures of total nutritional adequacy. In rare instances, tube feeding may become an unavoidable temporary expedient in anorexic patients who have become severely deteriorated nutritionally. The liquid mixtures described above may be used. Oral feeding always should be

resumed as soon as possible because the adverse psychological effects of tube feeding may in itself sustain anorexia.

Untoward Effects of Injudicious Diet Programs

The need for individualization is as important with diet therapy as with potent pharmaceuticals. Therapeutic nutrition can act as the proverbial two-edged sword. If not prescribed with proper judgment, severe complications may be produced. The requirements for each individual patient must be calculated separately. In addition, the state of the disease process must be considered. For example, a very high protein diet normally is indicated for the treatment of diseases of the liver. It is well documented that liver disease causes defective protein synthesis and other abnormalities of protein metabolism. Experimental liver disease is most readily induced when the diet is deficient in proteins. There are some patients with cirrhosis of the liver and chronic hepatitis, however, who are sensitive to high protein diets. Hepatic coma occasionally has been initiated by the indiscriminate use of very high protein diets. Protein restriction is mandatory if hepatic coma is present. A premature fatality may be provoked by an unwise persistence in forcing a high protein diet upon such patients.

"Milk-Alkali" Syndrome

Another example of an untoward effect produced by the overenthusiastic application of a dietary regimen without careful observation of the patient occurs in the case of peptic ulcers. The excessive administration of calcium, principally in the form of milk, and of absorbable alkalis, at times has led to the development of the "milk-alkali" syndrome. This syndrome is characterized by hypercalcemia without hypercalciuria, renal insufficiency and azotemia, with or without alkalosis. Metastatic calcification, nephrocalcinosis and renal calculi occasionally occur in sensitive individuals. Upon interdicting milk and absorbable alkalis, the hypercalcemia and azotemia rapidly disappear, though metastatic calcifications may persist.

Indications for More Lenient Diets

Rigid dietary restrictions probably are imposed upon patients far more often than actually is necessary. Recent studies have proved that fat is not as harmful in liver disease as once was believed. The current trend toward moderate fat diets makes it much easier to achieve adequate protein, calorie, vitamin and mineral nutrition. An analagous situation applies to the treatment of sprue, for which it recently has been shown that a moderate fat diet may be superior to the very low fat diets previously prescribed. In certain cases of gallbladder disease, very low fat diets can lead to stasis within the gallbladder, thus providing a superior environment for calculi formation and aggravating

a chronic cholecystitis. Moderate fat diets that stimulate the flow of bile often are of benefit in patients with chronic gallbladder disease.

It is becoming apparent that the majority of diets for patients with chronic peptic ulcer are unnecessarily severe. Certainly the irritation to the ulcer from many fruits and vegetables cannot be as great as was heretofore claimed. Except for the very acute stages, there probably is no need to alter significantly the texture of foods. Much of the patient's difficulty comes from a feeling of anxiety regarding the texture of his food. Patients should be reassured and should be encouraged to resume as early as possible a diet in which the permitted foods are consumed in normal amounts in their usual texture. It is my impression that more liberal diets, by providing a more pleasant situation at the dining table and by decreasing tension about food with its adverse psychologic and physiologic effects, will be helpful in the management of the average cases of peptic ulcer after the acute stage. Such diets undoubtedly would facilitate the creation of menus that fulfill all nutritional requirements.

The time has come to critically reevaluate the diets used for the treatment of gastrointestinal disturbances in order to expose and correct those diets which have been overzealously formulated and needlessly restricted in the content and preparation of foods.

Uniform, Simplified Nomenclature

It is appropriate to insert here a plea for the development of a simple and uniform diet nomenclature in gastroenterology. Numerous, often obscure terms are seen on the diet order sheets for gastroenterological patients. These include "ulcer diet", "gallbladder diet", "liver diet", "diarrhea diet", "constipation diet", "Sippy diet", "modified Sippy diet", "nonirritating diet" and so on. Designating diets after a pathological condition is undesirable. Such names do not make apparent the characteristics of the diet and they convey the impression that the diet is specific for a condition. The basic principles behind the diet are obscured. The same title may imply to different individuals' somewhat dissimilar diets. Then too, naming diets after a disease can be psychologically traumatic to the patient who constantly is reminded of his illness. The vagueness of certain terms is illustrated by the title "nonirritating diet". For some this signifies a bland diet, while others may interpret it to mean a low residue diet.

Designating diets after particular individuals or after specific diseases increases the possible number of diets. This causes diet therapy of gastrointestinal diseases to appear to the general practitioner more formidable than it actually is. The title of a diet should be specific and should indicate the nature of the nutritional therapy being prescribed. Terminology should be simplified and unnecessary duplication avoided. The term "bland diet", for

example, may be used whenever prescribing for digestive disturbances which respond to diets which are chemically and mechanically nonirritating.

Outlining the Diet to the Patient

When outlining a diet, it is essential to tell both the patient and his family just what he may eat. It is not enough to enumerate to the patient only the foods that must be avoided. Nutritional imbalance and dietary invalidism often are engendered by unwarranted fears of certain foods which, in reality, are perfectly innocuous for the disease state. To insure that a diet is not only the optimal one for the pathology present but also one that is nutritionally balanced, the information regarding the diet must come in detail from the physician or dietitian. The failure to spend the time necessary to give a secure and positive education to patients and their families has permitted quacks and food faddists to flourish and to prey upon the sick.

The importance of approaching a normal diet in every possible way in the treatment of gastrointestinal diseases cannot be overemphasized. It is becoming increasingly apparent that when formulating diets for the majority of gastrointestinal disorders, it frequently is possible to approximate a normal diet, certainly in composition and to a great extent in texture and quantity. This is imperative if secondary nutritional deficiencies and other deleterious side-effects are to be avoided.

Psychological Aspects of Therapeutic Nutrition

The too ardent application of dietary regimens by some physicians has not only led at times to iatrogenic malnutrition and other serious complications, but also to serious psychogenic disturbances, disruption of family patterns and manner of living and to what, in general, can be termed "dietary invalidism".

Of special importance in the dietary management of gastrointestinal diseases is the recognition that a significant percentage of the chronic digestive disturbances seen in practice are ailments associated with emotional disturbances and anxiety tension. These include peptic ulcer, mucous colitis, irritable colon, ulcerative colitis, biliary dyskinesia, pylorospasm, cardiospasm and the numerous functional disorders which manifest themselves as "dyspepsia".

It is essential for the patient to have peace of mind when eating and to avoid worry, rushing, fatigue and general emotional upsets at this time. Controversial and unpleasant subjects should not be discussed at the dining table. One must try to avoid increasing tension by prescribing a diet which is psychologically disturbing to the patient. If possible, the dietary regimen should be made simple. An undue fear regarding the consequences of dietary deviations should not be instilled in the minds of the patient and his family, for

this in itself conceivably could result in anorexia and functional gastrointestinal symptoms. Finally it may be noted that any diet which creates nutritional deficiencies, can by this mechanism both produce and exacerbate nervousness, irritability and emotional instability.

Summary and Conclusions

In this paper I have reviewed several of the important relationships between nutrition and gastrointestinal disease. The overlapping of symptoms and signs resulting from nutritional deficiency with those arising from gastrointestinal diseases has been emphasized. Accurate differential diagnosis is essential for optimal therapy.

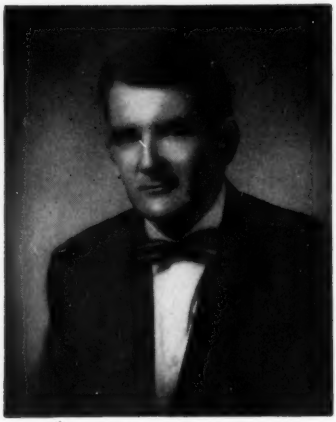
Diets for gastrointestinal diseases must be adequate in every respect. They not only must supply the daily needs of the body, but must compensate for current losses, such as by vomiting, diarrhea and ineffectual absorption, and for previous depletions. Although the foodstuffs in the diet require modification in texture, consistency and quantity per serving, the total qualitative and quantitative requirements for good nutrition must never be sacrificed. Iatrogenic malnutrition consequent to unwise diet planning still occurs, though it nearly always is preventable.

The regimen for a patient with gastrointestinal disease should be individually planned. He must be told what to eat as well as what not to eat. Lack of nutrition knowledge on the part of the patient, together with unwisely instilled fears, has caused inadequate diets to be consumed with a consequent prolongation of invalidism. Practical methods of overcoming the serious problem of anorexia have been presented. The psychological aspects of nutrition and gastroenterology also have been reviewed.

A plea has been made for a more simplified and uniform nutrition terminology among gastroenterologists. There is an urgent need for the leading gastroenterological organizations to form a committee on nutrition to review diet nomenclature. A simplified, orderly and specific system of designating diets for patients with digestive disorders would help to ensure successful nutritional therapy for these individuals.

Disorders of the gastrointestinal tract which are due to dietary deficiencies will respond promptly to replacement therapy. The treatment of gastrointestinal diseases which are not of a nutritional etiology will be aided greatly by a wisely calculated diet which is aimed not only at the specific symptoms and anatomical damage, but also at providing a general therapeutic nutritional regimen. The latter will increase healing power and can shorten notably the duration of convalescence.

The judicious and perceptive application of a diet program will bring rich rewards to both the gastroenterologist and his patient.



President's Message

Our Third Annual Convention will be at the Roosevelt Hotel in New York City, October 15, 16 and 17, 1956. An exceptional program has been arranged for the Convention and the Postgraduate Course that you will not want to miss. The Ladies Auxiliary has planned a schedule of activity for our wives, complete with social, recreational and educational outlets. I think she will want to attend. Be sure to bring her.

All of the Trustees and Governors are urged to come early as many preliminary committee arrangements have to be made on Friday and Saturday, immediately preceding the Convention. Issues most vital to our organization are scheduled to be voted on and must be thoroughly discussed, that is, the institution of chapters and rules for their management and the provision for active members to advance to Associate Fellowship by attending prescribed postgraduate courses. Furthermore, I hope that at this or an early meeting the College will set definitely the requirements for maintenance of Fellowship. No other specialty group requires continued training after certification in the designated specialties. I trust that the American College of Gastroenterology will be the first to require such continued specialty training for maintenance of Fellowship.

I. T. Nif

NEWS NOTES

New Fellowship Keys

New Fellowship keys for *Fellows* of the American College of Gastroenterology have been authorized by the Board of Trustees. An illustration of the new key is at the left.

Fellows may order the new keys from the headquarters office, 33 West 60th Street, New York 23, N. Y., at $10.00 each including federal tax and shipping charges.

The reverse side of the key will be engraved with the name and date of election to Fellowship. Send your orders in today.

In Memoriam

We record with profound sorrow the passing of Dr. Samuel S. Berger, of Cleveland, Ohio, Fellow and Dr. L. Winfield Kohn of New York, N. Y., Life Fellow of the American College of Gastroenterology. We extend our deepest sympathies to the bereaved families.

ABSTRACTS FOR GASTROENTEROLOGISTS

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GASTROINTESTINAL TRACT

THE UPPER MIDLINE ABDOMINAL INCISION: Millington O. Young. Northwest Med. 54:1121 (Oct.), 1955.

The experiences of various surgeons are quoted, and they are all in agreement concerning the advantages of this incision. These are simply: increase in exposure, decrease in operating time, and decrease in morbidity. The xiphoid process can be resected for still greater exposure especially of the left subdiaphragmatic space thereby facilitating the repair of a diaphragmatic hernia. For gastrectomy and cholecystectomy the author has not found it necessary to extend any incision below the umbilicus. The foregoing advantages plus the lack of technical difficulties suggest that the use of the upper midline abdominal incision, with or without resection of the xiphoid, is indicated much more often for all types of upper abdominal surgery.

CHESTER S. SVIGALS

POSSIBLE RECURRENT SECONDARY OMENTAL TORSION: Orland B. Scott. Northwest Med. 54:1121 (Oct.), 1955.

The author cites a case report of a 44-year old man who had been observed for a period of 9 years for a chronic upper abdominal complaint which was suspected to be due to either cholecystitis or a duodenal ulcer. At age 14 the patient had sustained a fracture of the right clavicle and an undiagnosed injury of the right lateral chest wall. A sudden exacerbation of the abdominal pain led to a diagnosis of acute cholecystitis and exploration on the following day. The operative findings consisted of a firm omental mass adherent to the right lateral abdominal wall. The mass was twisted at the base, and there were present hemorrhagic changes secondary to infarction. The pathological diagnosis was infarct of the omentum. The patient noted a marked decrease in his symptomatology following resection of the involved omentum.

The author speculates that an omental

adhesion had formed at the site of the previous right lateral chest injury, and this was responsible for the secondary torsion and infarction which may have been occurring intermittently during the 9 years prior to the episode leading to surgery.

CHESTER S. SVIGALS

ACUTE AND CHRONIC JEJUNOGASTRIC INTUSSUSCEPTION: William S. Caudell and C. Marshall Lee, Jr. New England J. Med. 253:635 (13 October), 1955.

By jejunogastric intussusception is meant a protrusion of the jejunum into the stomach following gastroenterostomy or else partial gastrectomy. Either the afferent, or efferent, or both loops may invaginate into the stomach. The condition is rare, but over 100 cases have been reported; the efferent in about three-fourths of the cases, the afferent or both with about equal frequency in the remaining fourth. The condition may be recurrent and selfreducing; it may not be demonstrated by x-ray after an attack has subsided; or it may cause permanent obstruction relieved by operation or resulting in death of the patient. Whenever vomiting or epigastric pain occurs in a patient who has had a gastrojejunostomy, recent or old, with or without a subtotal gastrectomy, this mechanical disturbance should be considered. If the diagnosis is made by prompt x-ray examination, and vomiting persists, it should be assumed that the process is acute and irreducible and prompt surgical intervention undertaken before gangrene of the involved bowel occurs. The cause of the condition is not known. The authors review a number of theories. Neither marginal ulcer nor polyps appear to be present with enough frequency to be incriminated as usual predisposing factors. In the acute type, when the neck of the intussusception is caught in the gastrojejunal stoma, it becomes fixed. In the usual type of partial gastrectomy (Billroth type II) when the obstruction becomes complete at the neck no intestinal fluid can return to the stomach, and bile, if it was previously present, is no longer vomited. Congestion of the loops can lead to vomiting of enough reddish brown fluid to simulate bleeding peptic ulcer. Tenderness and muscle guarding are not as great as might be expected, a clinically palpable mass was present in one-third of the cases. The authors discuss the details of the x-ray findings. The diagnosis of the chronic recurrent cases is difficult. The roentgenologist may be fortunate enough to make the diagnosis if the patient is seen during an episode. It should be sought for during the period of distress, and also in case of malfunctioning stoma. The type of operative treatment to be employed is discussed by the authors.

SAMUEL L. IMMERMAN

STOMACH

DUODENAL ATRESIA AND STENOSIS: Roy T. Tanoue. Hawaii M. J. 15:21 (Sept.-Oct.), 1955.

Duodenal atresia and stenosis is congenital and must be recognized early or the mortality is formidable. Surgery carries with it an immediate postoperative mortality of 75 per cent. More cases can be salvaged surgically providing adequate preoperative care is not neglected.

Diagnosis is made from the following: 1. Vomiting from the first day of life and continuing into second day. 2. Flat and upright x-ray films of the abdomen. 3. Barium may be harmful and should be removed after examination.

Treatment—immediate surgery. If obstruction is proximal to ampulla of Vater do a gastrojejunostomy. If it is distal to the ampulla do a duodenojejunostomy. Postoperatively, look to proper use of parenteral fluids. With the return of bowel movements and bowel sounds, may start use of glucose in water. Small transfusions to maintain blood count, plasma and protein levels.

The author's series showed a mortality rate of 71 per cent.

LOUIS K. MORGANSTEIN

TREATMENT OF PEPTIC ULCERS WITH "ROTER" TABLETS: Roderick R. Hamilton. Brit. M. J. 4943:827 (1 Oct.), 1955.

"Roter" Tablets were first introduced into England from Holland in 1948. The present study was made by the author to determine the efficacy and possible toxic effects of the drug since it contained bismuth subnitrate. The tablets contain 50 mg. of bismuth subnitrate,, magnesium carbonate 40 mg., soda bicarbonate 200 mg., calamus 25 mg., aromatic bitters and frongula which has a mild laxative action similar to cascara. The dosage used was two tablets, three times daily, after meals, for three weeks and then one tablet after meals for three months. Where recurrences were frequent a maintenance dose of two tablets daily was taken for a full year.

There was a satisfactory response in 90 per cent of cases. In the 10 per cent of failures, no form of medical treatment was effectual and surgery was advised. The 90 per cent of satisfactory cases were all ambulatory and were not on a restricted diet. "Roter" tablets do not affect the relapse rate. There was a 50 per cent relapse at the end of one year in those cases only receiving three months of treatment. This rate may possibly be reduced by a prolonged period of treatment.

Possible toxic effects from the use of "Roter" Tablets arise from the conversion of the subnitrate to nitritis with the formation of methemoglobinemia. While there were no toxic manifestations in the cases treated by the author, the literature contains numerous such references. However these cases mostly occurred in infants from one week to one and one-half years of age and especially occurred in the presence of diarrhea.

ALEXANDER ZABIN

SURGERY IN PEPTIC ULCER: R. Morton Bolman and Robert P. Lloyd. Med. Times 83:961 (Oct.), 1955.

The authors present their criteria of surgical selection and their system of surgical management of the peptic ulcer patient.

Fifteen to twenty per cent of all peptic ulcer patients require surgery.

In their technics the authors are guided by the physiology of gastric secretion; 45 per cent of the free hydrochloric acid production is antral, 45 per cent cerebral, and only 10 per cent is intestinal. Only through total gastrectomy is it possible to remove all the acid-producing cells. However by doing a 50 per cent antral gastrectomy and a vagotomy the authors believe they have abolished 90 per cent of the acid-producing factors.

In the opinion of the authors this combined technic gives better end results than the conventional subtotal gastrectomy alone. The very often encountered postoperative "small stomach syndrome" is thus avoided. The patients are able to eat much sooner and lastly the possibility of a recurring ulcer is kept to a minimum.

The authors share the common opinion, that any gastric ulcer—because of its potential malignancy—which has not completely healed after 3 weeks of medical management, should be subjected to radical surgery. Indications for surgery are as follows: 1. perforation—if clinically possible the 50 per cent gastric resection is the operation of choice. 2. obstruction, 3. failure of medical management, 4. intractable pain—especially if any penetration is present, 5. hemorrhage, 6. inability to go through with and 7. refusal of the patient to follow medical management. Indications 6 and 7 should be weighed very carefully by the surgeon.

Finally the authors describe the different types of marginal ulcers, and the respective surgical technics.

HANS J. JOSEPH

PRELIMINARY OBSERVATIONS ON HEMIGASTRECTOMY WITH SUBDIAPHRAGMATIC VAGOTOMY FOR THE AVERAGE CASE OF CHRONIC DUODENAL ULCER: Stanley O. Hoerr. Cleveland Clin. Quart. 22:172 (Oct.), 1955.

In a series of 120 cases which the author reports, the surgical procedure of hemigastrectomy with subdiaphragmatic vagotomy yields very good results but not enough

time has elapsed to state definitely to what extent if any late recurrences may be expected.

The operative procedure has a low incidence of severe side reactions as compared to some other gastric procedures, notably gastrectomy (operative mortality was higher for this procedure than the one it has supplanted, vagotomy with posterior gastroenterostomy in cases where the indications were similar).

The study covers two years. No recurrent ulceration has been noted thus far; long term study is needed for fuller evaluation. The author still has to decide on the best procedure for the average case of chronic duodenal ulcer.

IRVIN DEUTSCH

PEPTIC ULCER IN MILITARY PERSONNEL: Benjamin H. Sullivan, Jr. and Eugene L. Hamilton. U. S. Armed Forces M. J. 6:1459 (Oct.), 1955.

The authors emphasize the increased incidence of peptic ulcer in the United States Army in recent years.

In 1953 the admission rate among officers in Europe was 75 per cent greater than the rate among officers in the Continental United States. The rate among the enlisted men in Europe was more than twice the rate of enlisted men in Continental United States.

JOHN E. COX

CLINICAL PICTURE OF PYLORIC CHANNEL ULCER: Julian M. Ruffin, David H. Johnston, Donald D. Carter and George J. Baylin. J.A.M.A. 159:668 (15 Oct.), 1955.

The authors call attention to the fact that peptic ulcers located in the pyloric channel give rise to symptoms totally unlike the ordinary duodenal ulcer and are often entirely missed.

Their study includes an analysis of the clinical features of 100 consecutive patients with channel ulcer proven by x-ray. The sex ratio was 3 males to 1 female and the ages varied from 19 to 83 with most of the cases occurring between ages 30-60. For comparison the clinical features of an additional 100 consecutive patients having an uncomplicated duodenal ulcer were studied.

The clinical features of channel ulcer were nausea and vomiting, upper abdominal pain and marked weight loss. The commonest diagnostic errors in this series were in mistaking channel ulcer for psychic vomiting or carcinoma of the stomach. Less commonly it was confused with gallbladder or pancreatic disease.

Suggested treatment includes mandatory hospitalization with intensive ulcer regimen including overnight gastric suction. Surgery was necessary in 38 per cent of cases.

W. K. BILLINGSLEY, JR.

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS: John L. Savage. Quart. Bull. Northwestern Univ. M. School 29:236 (Fall), 1955.

A report is presented of 61 cases of congenital hypertrophic pyloric stenosis which were subjected to surgery. Fifty of these infants were males. The etiology is unknown. In all instances unsuccessful conservative antispasmodic treatment had been given for a few days to a few weeks prior to surgery. Gastric waves or a palpable tumor was felt in 80 per cent of cases. Barium swallow was employed in 26 infants. Preoperatively almost all received parenteral fluids. The anesthesia of choice was open drop ether. A small catheter was placed in the stomach preoperatively in order to empty the stomach prior to surgery. Seven different surgeons performed the operations with the procedure of choice being a longitudinal section of the hypertrophied pyloric muscle. There was no mortality. Feedings first of water then milk formula were started 4 hours after surgery.

BERNARD J. FICARRA

LIVER AND BILIARY TRACT

BRILL-SYMMERS DISEASE LOCALIZED IN THE SPLEEN, LIVER AND RECTUM: B. Wissmer, H. Dubois-Ferriere, E. Naz and P. Wettstein. Arch. mal. app. dig. 44:273 (March), 1955.

The authors are reporting a rare case of Brill-Symmers Disease which involved a 56-year old female. The affection had started with diarrhea, progressively becoming bloody, which lasted for a period of 4 years despite all types of treatments tried in her country. This had lead to a cachectic condition with ascites. At the end of 1954, an enormous splenomegaly was found, without hepatomegaly or adenopathy. A rectosigmoidoscopy showed an ulcerative proctitis, and the biopsy of the rectal mucosa revealed a strong infiltration with lymphatic follicules. An important lymphomonocytosis of the blood was also observed. The actual diagnosis was only made after splenectomy. The liver biopsy showed an invasion of the liver, which, nevertheless developed its hypertrophy only after removal of the spleen. Under the effect of roentgentherapy, the liver returned to its normal size. Following the operation and roentgentherapy there was a dramatic change in the condition of the patient. She regained 19 kgs., but 3 months later she had a recurrence of diarrhea provoked by the rectal localization of the Brill-Symmers Disease. A few sessions of roentgentherapy on the rectosigmoidal region brought a lasting "cure" to those troubles which were absolutely resistant to other therapeutics. One year and a half after the operation, the patient is in perfect health, has a liver of normal size and function, presents no adenopathy and shows a normal blood picture.

RESEARCH INTO THE SURGERY OF THE UPPER BILIARY CONFLUENT AND THE HEPATIC CANALS: C. Cournaud. La Presse Med. 63:669-674, 1955.

The upper biliary confluent and the hepatic canals can be easily operated on. A preoperative cholangiography shows up the details of the main anatomical dispositions of this confluent which are considerably at variance with the usual descriptions (in 51 per cent of cases only is there a right and left hepatic canal).

After resection of the confluent, restoration of biliary continuity must be considered. The surgeon has three methods at his disposal: termino-terminal suture of one of the hepatic canals with the distal segment of the main tract the other undergoing a jejunal derivation; jejunal derivation of the hepatic canals by means of a Y-shaped joint (Roux type) set up on the hilum of the liver: intrafissural cholangiojejunostomy; peripheric derivation of the right biliary tract (at the level of the right angle of the liver), and the left biliary tracts (at the level of the anterior portion of the left lobe): peripheric cholangiojejunostomy.

The indications for these different technics are given in detail.

GUY ALBOT

ACUTE CHOLECYSTITIS: Alexander E. Pearce. Pennsylvania M. J. 58:598 (June), 1955.

The author proposes that surgery can be done at any time after the diagnosis is clear and the patient properly prepared. He refutes the policy of nonintervention in acute cholecystitis and denies that it is necessary to operate early in such cases (within 72 to 96 hours). He abolishes the concept that surgery in acute cholecystitis from 4 to 12 days after the inception of the disease is undesirable.

A series of 88 consecutive cases of acute cholecystitis seen by one surgeon over a four-year period is presented. Preparation by relief of pain, administration of fluids, use of suction if needed, the value of cholecystography and, when necessary, gastrointestinal series and hepatic function tests, and the care of concomitant disease as pre-

paration for surgery are described. Selection of the time for surgery after usually one night, occasionally two nights, and rarely more time, is made so that the best concentrated attack on the disease may be made, viz., cholecystectomy.

JACOB A. RIESE

HEPATIC COMA: A CLINICAL AND PATHOLOGIC STUDY: William T. Foulk, Hugh R. Butt, Maurice H. Stauffer, Archie H. Baggenstoss and John B. Gross. Gastroenterology, 29:171 (Aug.), 1955.

The authors studied 52 consecutive patients who were seen in hepatic coma at the Mayo Clinic. The clinical or pathological diagnosis was cirrhosis in 23 of these patients; in nine patients the diagnosis was hepatitis; in four it was biliary cirrhosis secondary to common-duct stricture or stone; in 11 it was obstructive jaundice, and in five it was neoplastic malignant involvement or abscess of the liver.

Hemorrhage, infection, paracentesis and surgical procedures appeared to be responsible for the onset of coma in most cases.

The basic management of hepatic coma consists of attention to slight changes in the patient's clinical status, good nursing care, intravenous administration of 2 to 3 liters of a 5 per cent glucose in water, vitamins, especially thiamine (50 to 100 mg.), and nicotinic acid (200 to 500 mg.), and synthetic Vitamin K 5 mg. daily. Repeated small blood transfusions (250 cc.) are advised in the absence of hemorrhage; in the presence of bleeding proportionately more blood replacement is necessary. Fluid and electrolyte balance must be carefully watched with special emphasis on potassium levels. If cortisone or ACTH is given to the patient in hepatic coma, its use must be continued for long periods. The authors have observed patients in whom clinical evidence of impending coma apparently disappeared when a diet low in protein was given.

The prognosis is poor in cases of hepatic coma because the genesis of the condition is obscure. Death occurred in 47 of the 52 cases. However, the factors responsible for the favorable outcome in the five cases were obscure.

SAMUEL M. GILBERT

ARTERIALIZATION OF THE HUMAN LIVER FOLLOWING PORTACAVAL ANASTOMOSIS: S. Austin Jones, Telfer B. Reynolds, Ernest B. Schultz and George Gregory. West. J. Surg. pgs. 574-579 (Sept.), 1955.

The authors hope that this report of a single case of a patient with Laennec's cirrhosis, in whom arterialization of the stump of the portal vein was done following portacaval anastomosis, would stimullate interest in a procedure which may improve liver function as well as lower portal pressure. A brief review of the vascular anatomy and physiology of the liver is given, bringing out the fact that in the normal liver 70 per cent of the volume of the blood to the liver comes from the portal vein, while 30 per cent comes from the hepatic artery. This means that about 60 per cent of the oxygen supply comes from the portal system, and 40 per cent from the artery. In cirrhosis, the hepatic vein carries only 30 per cent of the blood and about the same in oxygen, while the artery carries 70-80 per cent of the volume, and about 70 per cent of the oxygen.

Cardiac catheterization, with the catheter being passed into the inferior vena cava and "wedged" into the liver through the right hepatic vein, was done. This was left in place. The right gastroepoploic artery was anastomosed into the portal vein stump, while the portal vein was shunted into the inferior vena cava through a vessel graft. The patient made an uneventful recovery; subsequent follow-ups showed that she was at least as good as before surgery, and esophagrams done the following month revealed a normal esophagus.

In the discussion, the authors point out that although only one case has been done, it is of interest, and might be further explored. They state that the technic could be improved upon, and offer suggestions for that improvement.

OPERATIVE CHOLANGIOGRAPHY: A REVIEW AND EVALUATION: Milton F. Popp. Indiana State M. A. 48:996 (Sept.), 1955.

Direct operative cholangiography is a procedure of value. It does not increase morbidity or mortality and is very helpful in the detection of unsuspected common duct stones. Secondary common duct operations are thus avoided in addition to the sequela of subsequent stricture. The diagnosis of anomalies and extraductal and noncalculous obstructions is often possible.

Statistically a possibility of missing common duct stones despite operative probing is significantly great. Ten to 23 per cent of patients were found to have common duct stones despite previous operative search.

The operative time is lengthened by 15 to 20 minutes but the author feels the diagnostic importance of the procedure should invite surgeons and radiologists alike to become proficient in its use.

JOSEPH E. WALTHER

NUTRITIONAL FATTY LIVER—Kwashiorkor: Marcel Tuchman. Med. Times 83:887 (Sept.), 1955.

Nutrition has been considerably neglected as a factor in etiology. The influence of nutritional inadequacies upon fat deposition in the liver parenchyma of a pathological nature is explored in this article.

A newly discovered disease in the tropics where it is widespread, has been named "kwashiorkor". It affects infants and young children by predilection, with a high mortality rate. Now it seems certain that a similar condition exists in Germany, named "Mehlnahrschaden", while the same syndrome is known as "nutritional edema" in South America, India, and the United States. Kwashiorkor is characterized by: retarded growth; skin and hair pigment alterations; edema; liver changes including fatty infiltration, cellular necrosis, and fibrosis. Without proper dietetic substitution therapy there is a high mortality. Often a variety of dermatoses form part of the picture.

Kwashiorkor belongs to that large class of disorders with a common etiology of protein malnutrition. Young children fall victim to it as a result of a prolonged monotonous, deficient animal-protein, excessive carbohydrate dietetic regime. Dramatic improvement follows taking of milk-proteins, but vitamin deficiencies seem to be a negligible factor. However, associated infections and infestations must be energetically treated.

REGINALD B. WEILER

LIVER FUNCTION AND HEPATIC COMPLICATIONS IN PATIENTS RECEIVING CHLORPROMAZINE: Irvin M. Cohen and John D. Archer. J.A.M.A. 159:99 (10 Sept.), 1955.

The use of chlorpromazine is occasionally complicated by the development of jaundice. In this paper the authors review a series of 89 patients being treated with thorazine for psychiatric illnesses of various types. Five patients developed jaundice. Serial liver function tests were obtained in most cases before, during, and after administration of the drug and careful physical examinations were done at like intervals. Statistics were compiled correlating age, sex, dosage of drug, duration of therapy, allergic history and route of administration of the drug.

The authors conclude that the development of jaundice is an expression of drug idiosyncrasy. The process is confined to the bile passages with sparing of the liver parenchyma. In general the investigation suggests that under ordinary circumstances chlorpromazine is not hepatotoxic and can be administered over long periods of time without undue risk.

W. K. BILLINGSLEY, JR.

DIABETES MELLITUS AND LIVER FUNCTION: Robert F. Bradley, Uffe Sagild and Fredy E. Schertenleib. New England J. Med. 253:454 (15 Sept.), 1955.

A study of 118 cases of controlled diabetes indicates that insulin treated patients do not develop hepatic disorders from the disease as has been formerly thought.

Using standard modern function tests, including bromsulfalein, 6.8 per cent of the group showed positive reactions, 10.8 per cent showed some degree of sulfalein retention, 3 cases 11, 12 and 13 per cent respectively.

The picture of controlled diabetes appears to be the direct opposite of uncontrolled diabetes, where livers, enlarged by fat deposits, glycogen deposits or a combination of both, show marked cirrhosis at necropsy or at needle biopsy.

The choline obtained from lean meats plus the insulin controlling carbohydrate metabolism, evidently prevent the accumulation of fats and glycogen, thereby stopping cellular irritation that leads to cirrhosis.

In the series 16 patients gave abnormal liver findings of one or more positive tests. 6 gave two or more positive tests, and yet the duration of the disease had no bearing on the findings, patients with diabetic histories of 20 years, showed normal test responses.

From this study it can be assumed that hepatic disturbances stem from poorly controlled diabetes or from some other condition present with the diabetes.

J. Edward Brown

LIVER DECOMPRESSION BY COMMON BILE DUCT DRAINAGE IN SUBACUTE AND CHRONIC JAUNDICE: Alfred A. Strauss, Siegfried F. Strauss, Arthur H. Schwartz, William J. Tannenbaum, David D. Kram and Walter W. Masur. J.A.M.A 159:739 (22 Oct.), 1955.

Feeling that insufficient consideration had been given to surgical drainage of the common duct and decompression of the liver in the treatment of jaundice resulting from acute and subacute hepatitis on an infective basis, the authors evaluate their results in a series of 60 operative cases. Fifty-five cases operated made a complete recovery while five were not relieved of jaundice and died. While they admit that some of their recoveries might have occurred on medical therapy alone the authors feel that the recovery rate could not have been achieved by strictly medical means. All of the cases operated had had an adequate trial period medically and were in poor condition at the time of surgical intervention.

It has been the finding of these investigators that a certain percentage of hepatitis cases failing to respond to medical management will show in addition to hepatitis, inflammation of the extrahepatic ducts originating in the duodenum and that this inflammatory process produces an obstruction of the bile flow at the papilla of Vater. Several other interesting pathological findings including a severe infiltrating duodenal ulcer near the papilla of Vater producing ductal blockage are reported in this study.

Recurrent jaundice following common bile duct drainage means contraction and infiltration of the distal portion of the common bile duct and of the papilla of Vater due to connective tissue formation. The authors feel that the best operative procedure to relieve this type of jaundice is the one arm Roux-Y operation of Cole, Iraneu and Reynolds using a newly devised vitallium tube with sharp prong-like projections at the upper end which pierce the tissue surrounding the hilus of the liver making it almost impossible to dislodge the tube from its position.

W. K. Billingsley, Jr.

ATTEMPT AT SURGICAL TREATMENT OF CIRRHOSIS OF THE LIVER. Critical study of the "portalization procedure" with the hepatic artery: Lucien Leger, Guy Albot and Louis Vaille. La Presse Med. (5 Oct.), 1955.

The authors refer to their previous works reported in La Presse Médicale and dealing with such anatomical observations as they could make in the course of their surgical interventions on cirrhotic patients; they emphasize the role of the lymphatic participation, the frenquency of vesicular involvement which they assume to be, in certain cases, the original factor of cirrhosis, finally the part possibly played by venous thrombosis.

They particularly study the "portalization" of the hepatic artery, a procedure suggested by Soegesser and consisting in arterioportal anastomosis with ligation of the afferent trunk of the hepatic artery, of which a personal case is here described.

They point out how they were able to

demonstrate the failure in functioning of the phleboarterial anastomosis by means of postoperative splenoportographs and by postmortem examination showing that, even though the anastomosis might have remained permeable, it was not functionally operating, because undoubtedly an artery cannot work under a venous pressure, when deprived of the sphygmic impulse.

DUODENOBILIARY DYSKINESIA, DUODENOGASTROESOPHAGEAL REFLUX, DUODENOBILIARY ASPIRATION, FUNCTIONAL DISORDERS AND PHARMACODYNAMIC DISORDERS OF THE DUODENAL SPHINCTERS REVEALED BY NONOPERATIVE TRANSHEPATOVESICULAR RADIOMANOMETRY (PARESIS OF THE BULBODUODENAL SPHINCTER AND OF THE PYLORUS, SYMPTOMS OF FUNCTIONAL REFLUX OR BULBDUODENITIS): M. Kapandji. Arch. mal. app. dig. 44:(Sept.-Oct.), 1955.

All the duodenal sphincters, from the pylorus passing through the bulboduodenal sphincter (1st part of the duodenum), the medioduodenal sphincter (2nd part of the duodenum), Ochsner's sphincter (3rd part of the duodenum) as far as and including the more or less pronounced and fairly high bend of the duodenojejunal angle, affect the functioning of the biliary tract; but the latter also have an influence on the working of the various sphincters.

It has been possible for the author to study this synergy, this duodenobiliary couple, in quite a special way, through the biliary tract by the use of nonoperative transhepatovesicular radiomanometry.

Manometric hypertension through the biliary tract has enabled us to state that it did not only cause a precautionary contraction of the Oddi, but that this contraction was somewhat rare compared with the precautionary contractions of the duodenal sphincters such as the medioduodenal, the bulboduodenal, the Ochsner, or even the pylorus, and that there could be associated with these precautionary contractions those of Mirizzi's sphincter and even of the intrahepatic biliary channels. We thereby understood the defense mechanism of the duodenobiliary couple when faced with a brusque inrush of liquid, or hypercholeresis.

Finally we have described the images which, after administration of barium, are typical of pareses of the bulboduodenal and the pylorus during a functional disorder or bulboduodenitis.

Nonoperative transhepatovesicular radiomanometry has enabled us to study, through the biliary tract, certain novel aspects of duodenobiliopancreatic synergy and to note the high frequency of duodenobiliopancreaticgastric dyskinesia, responsible for functional disorders still ill-defined.

GUY ALBOT

SURGICAL TREATMENT OF PORTAL HYPERTENSION: Frank R. Denman. Texas J. Med. 51:697 (Oct.), 1955.

The author gives a review of the present conception of intra- and extrahepatic block in portal hypertension. The pathological anatomy and physiology is well described. Intrahepatic block is commonly due to some form of cirrhosis of the liver. The extrahepatic block is due to thrombosis, neoplastic processes, or congenital anomalies. Thrombosis may be of traumatic, inflammatory origin or may develop spontaneously. Extrahepatic block patients have a longer life-expectancy than the intrahepatic block group. Among the clinical symptoms gastrointestinal hemorrhage is the most serious one, causing a mortality of about 40 per cent one year following the first hemorrhage. Surgery cannot reverse the pathology, but only improve the symptomatology.

The indication for surgery has to be based on the general status, a plasma albumin at more than 36 mg. per 100 c.c., the absence of 4 + cephalin flocculation, a low prothrombin time, even if only as a result of Vitamin K therapy. Bromsulfalein and the presence of ascites have to be considered but are not of ultimate influence.

Surgery has to be divided in two groups: 1. to ablate the source of bleeding, 2. to reduce the portal hypertension.

To group 1. belong: Balloon tamponade; esophagoscopic injections; thransesophageal ligations and total resection of the gastroesophageal segment.

To group 2. belong: Splenectomy; splenic artery ligation; portacaval and splenorenal shunt procedures and ligation of the hepatic artery combined with splenic artery ligation.

The gastric resections for group 1; the portacaval shunt operations for group 2, in properly chosen patients afford the best result in the author's opinion.

HELMUTH NATHAN

PATHOLOGY AND LABORATORY RESEARCH

HEMOCHROMATOSIS: Yoshie Takagi. Med. Times. 83:256 (Mar.), 1955.

Hemachromatosis is a disease of unknown etiology in which body iron stores are markedly increased. The various iron pigments and the newer concepts of iron metabolism are reviewed. Iron appears to be absorbed by the mucosal cells of the gastrointestinal tract, where the controlling device appears to lie. In hemachromatosis, the excessive accumulation is probably due to a defect in the mucosal cells, which leads them to absorb more than the usual amount of iron. The increase may be slight, but over a period of many years, the iron accumulates in the body. There are three types of the disease: endogenous (idiopathic), exogenous (in anemic patients receiving transfusions), and nutritional (in the presence of various deficiencies).

There are three basic pathological features: deposition of hemosiderin, fibrotic changes, and cellular degeneration. The liver is the organ most commonly involved, and there is a Laennec type of portal cirrhosis, as well as an increased incidence of primary hepatic carcinoma. Diabetes mellitus occurs as a complication of hemochromatosis, and is an index of the damage to the islet cells of the pancreas; increasing insulin resistance may develop. All organs may be involved, and the total body iron of 4 to 5 gm. may be increased tenfold.

The maximum incidence is in males, between the ages of 40 and 60 and there is frequently a family history. It is characterized by four features: 1. Enlargement of the liver; 2. Pigmentation of the skin; 3. Diabetes mellitus; 4. Sexual hypopasia, with regression of secondary sexual characteristics. Diagnosis is confirmed by Fishback's skin test, Rou test of urinary sediment, biopsies of the liver, skin, or gastric mucosa, or one of the technics which demonstrate excessive iron.

Treatment is by repeated phlebotomies. Attempts have been made to limit iron absorption or to use chelating agents, but have not proven too practical.

ARNOLD L. BERGER

EXPERIMENTAL PSEUDOMEMBRANOUS ENTEROCOLITIS: Capt. Donald G. McKay, Lieut. Col. Robert M. Hardaway III, Lieut. George H. Wahle, Jr. and Capt. Robert M. Hall. A.M.A. Arch. Int. Med. 95:779 (June), 1955.

Experimental pseudomembranous enterocolitis has been produced in dogs by infusion of incompatible blood. These animals exhibited progressive shock, anuria, bloody diarrhea and coma before their death. The symptomatology closely resembled the human disease except that the profuse, watery diarrhea seen in man has not been observed in the dogs. The pathological changes are identical consisting of hemorrhagic necrosis of the superficial mucosa of the gastrointestinal tract, especially of the small and large bowel with pseudomembrane formation and thrombosis of the capillaries in the intestinal wall as well as in the kidneys, the liver, and the lungs. These findings do not support the idea that a change of the intestinal flora, especially the presence of resistant staphylococci, caused by the action of the antibiotics, is responsible for pseudomembranous enterocolitis. This concept has been previously questioned by the experience that this disease has been seen probably with equal frequency before the antibiotic era and that it is still observed in cardiac patients and other disorders where antibiotics have not been administered. On the basis of these animal experiments the conclusion is reached that pseudomembranous enterocolitis is produced by intracapillary thrombosis in connection with hemolytic processes or in the presence of malignancies or other conditions favoring blood clotting, and that the localization of the thrombi in the intestinal capillaries is conditioned by the stasis of the blood in the splanchnic bed associated with shock or abdominal surgery.

H. B. EISENSTADT

CHLORPROMAZINE IN MANAGEMENT OF NAUSEA AND VOMITING: Jose M. Torres Del Toro and Horace A. Albertson. Virginia Med. Monthly 82:306 (July), 1955.

Seventy patients, suffering from nausea and vomiting caused by a wide variety of conditions were treated with chlorpromazine (Thorazine). Excellent results were obtained in 78.6 per cent of the patients with the parenteral route of administration being used in most cases.

Side-effect was drowsiness. Precaution should be observed as withdrawal of depressing drugs or reduced dosage. After injections, keep patient in recumbent position for at least half an hour. There also has been reported some cases of jaundice.

WALLACE SPIGEL

THE ROLE OF NUTRITION IN GERIATRIC RESTORATION: Murray B. Ferderber. Pennsylvania M. J. 697:58 (July), 1955.

The writer compiles several observations from a county institution for aged and indigent near Pittsburgh. They are: 1. Some patients are tyrants, making demands for special foods. 2. Some used their disability as a weapon of pity to obtain what they wanted. 3. Some accepted their ill fortune as a pattern of normal living.

The author, from his experiences concludes the following: 1. Food for the aged should be simple, economical, well prepared and served at regular hours. 2. Best results are obtained by reduction of fats, reasonable amounts of carbohydrates and high protein diets. 3. Milk and its products are very valuable. 4. Fruits, cooked, baked or in pastries afford some pleasure. 5. High protein and high mineral diet prevent decubitus ulcers, incontinence, and demineralization of bones. 6. Vitamin therapy is unnecessary if nutrition is adequate, get sufficient sun, movement and productive recreation. 7. Body movement, exercise for the bed-fast patient and ambulation for those capable will assist in producing good nutrition.

LOUIS K. MORGANSTEIN

AGAMMAGLOBULINEMIA IN THE ADULT: Marvin Rosegan, Frank E. Trobaugh, Jr. and William H. Danforth. Am. J. Med. 19:303 (Aug.), 1955.

The literature abounds with reports on agammaglobulinemia. This disorder was at first discovered in male children but has since been reported also in adults of both sexes. Absence of serum hemaglutinins and low serum globulin with a high A/G ratio determined by the standard precipitation method of Howe will serve as screening tests of this disorder. The final diagnosis depends on paper chromatography. Symptomatology of this disorder varies greatly; however, there are persisting and recurrent infectious processes involving various systems of the body. Not so well known are cases where the gastrointestinal tract is mainly affected. They show nausea, vomiting, belching, heartburn, anorexia, sharp abdominal pains, fever, diarrhea and watery or bloody stool. Sigmoidoscopy may show easily bleeding friable mucosa. X-ray of the gastrointestinal tract may reveal small bowel changes suspicious of regional enteritis or sprue. No form of treatment will help these disorders except intramuscular injections of gamma globulin. Therefore, agammaglobulinemia must be added to the list of recurrent or persisting bowel disorders.

H. B. EISENSTADT

A NEW TECHNIC COMBINING SUCTION AND FEEDING FOR USE IN GASTRIC SURGERY: I. Ridgeway Trimble and John Nouri. J.A.M.A. 158:1361 (13 Aug.), 1955.

In order to supply an answer to a long standing need for a combined means of drainage and feeding after gastric operations, the authors have devised a method consisting of two polyvinyl tubes of small caliber (12F) tied together and inserted before operation through one nostril down into the stomach. If an end-to-side anastomosis is being made between the stomach and jejunum, the tubes are drawn through the open gastric stump and after the posterior rows of sutures have been completed, the three silk ties are cut thus separating the catheters. The catheter dyed red at

both ends and stamped with the word "suction" is led down about 20-25 cm. into the proximal limb in order to drain duodenal, pancreatic and biliary secretions and take pressure off the closed duodenal stump. This catheter has additional holes in order to drain the gastric stump. The other catheter dyed blue at both ends and stamped with the word "feeding" is led into the distal limb of the jejunum for 20-25 cm. and is used for giving water, salt, glucose and a liquid diet. It can also be used for suction if desirable. In the Billroth type of anastomosis the method is also applicable, the only difference being the withdrawal of the suction tube into the stomach instead of the duodenum.

On the day of operation and on the day after operation the entire fluid, glucose and electrolyte requirements are given through the jejunal tube. Forty-eight hours after operation a high protein, high carbohydrate liquid diet is given through the feeding tube. The feeding tube is usually kept down 4-6 days at which time oral feedings are given. Immediately after operation the red tube marked "suction" is connected to gentle bedside suction. During the next 24-48 hours this tube can be clamped off and when no longer necessary can be withdrawn without removing the feeding catheter.

The advantages of such a method are obvious.

WM. K. BILLINGSLEY, JR.

BOOK REVIEWS FOR GASTROENTEROLOGISTS

PLASTIC REPAIR OF GENITOURINARY DEFECTS: George Bankoff, M.D., F.R.C.S. (Ed), F.R.F.P.S., Honorary Surgeon, Italian Hospital, London, Formerly Associate Professor of Surgery, Plastic and Reconstructive Surgery, Georgetown University Medical School, Washington D.C., Honorary Surgeon, St. Josephs Hospital, Manchester, Chief Surgeon, Plastic Department, George Eastman Institute, Rome, etc., etc. 354 pages, illustrated in black and color. Philosophical Library, New York, N. Y., 1956. Price $17.50.

A well written and illustrated book dealing with genitourinary defects and their repair. There is also a chapter on sterility and impotence which the genitourinary specialist, the gynecologist and the general practitioner will find of value. However, the volume is written especially for the genitourinary surgeon.

THE HUMAN ADRENAL CORTEX—VOLUME VIII. Editors for the Ciba Foundation —G. E. W. Wolstenholme, O.B.E., M.A., B.A., B.Ch. and Margaret B. Cameron, M.A., A.B.L.S. Part I — Dr. Gregory Pincus, Chairman; Part II — Dr. George W. Thorn, Chairman. 665 pages, illustrated. Little, Brown and Co., Boston, Mass., 1955. Price $10.00.

A profuse and scholarly dissertation on the adrenal cortex by numerous research workers interested in endocrinology and allied physiological subjects.

Practitioners of medicine and teachers of physiology and endocrinology interested in steroids and ketosteroids in man will find this volume a *vade mecum*.

THE INTERPRETATION OF THE UNIPOLAR ELECTROCARDIOGRAM: Gordon B. Meyers, M.D., Professor of Medicine, Wayne University College of Medicine, Head, Department of Medicine, City of Detroit Receiving Hospital. 164 pages, illustrated. The C. V. Mosby Co., St. Louis, Mo., 1956. Price $4.75.

Another Mosby manual which will be appreciated by the medical student, general practitioner and the graduate student. In this well written and illustrated work, the reader will find electrocardiographic interpretation simplified. It is highly recommended as a useful addition to the physician's library.

THE LIVER AND CANCER — A NEW CANCER THEORY: Kasper Blond, M.D., F.I.C.S., with a foreword by E. Stanley Lee, M.S., F.R.C.S. John Wright & Sons, Ltd. Bristol, (Williams and Wilkins Co., Baltimore) 1955. Price $6.50.

Interesting, though a little far-fetched, is this monograph on the liver and cancer. Carefully reading the many pros and cons gives one a general idea as to what the possibilities are in disseminating cancer cells in the blood stream, while in other cases, such as lymphosarcoma, disseminating the cancer through the lymphatic vessels.

On page 130, the author cites a very unique case of cancer of unrecognized or rather undiagnosed primary origin and surgeons are often puzzled on opening an abdomen which shows advanced metastasis but no primary focus. Such was the case of the late Senator Robert A. Taft, who died on July 31, 1953.

Chapter 48 — "Is Cancer a Preventable Disease-" — should be read by all those who are interested in statistics.

SPLENO-PORTOGRAPHIE: Lucien Leger, Foreword by Henri Moncor. 166 pages profusely illustrated. Masson et Cie, Paris, France, 1955. Price 1,600 fr.

One of a series of monographs published by Masson and Co., Paris, dealing with visualization of the spleen, liver, kidneys, etc., by means of an opaque medium. This

is an ingenious and useful method in determining the normal or abnormal state of these organs plus the blood vessels. The method consists of injecting 30 c.c. of Diodone in 4 or 5 seconds and taking an x-ray film immediately followed by serial films at intervals.

Study of the developed films reveals normal or abnormal state of the kidney, spleen, liver and blood vessels, thus determining preoperative diagnosis or when question arises after operation.

Radiologists reading French will find this little book of immense value.

A.B.C. FUR ZUCKERKRANKE (THE A.B.C. OF DIABETES)—7TH REVISED EDITION: Prof. Dr. F. Bertram, 76 pages. George Thieme Co., Stuttgart, Germany, 1955. Price DM 4.20.

This little treatise written in German for the benefit of the diabetic, describes in detail the life cycle, the medical, diabetic and other relevant facts dealing with the pitfalls and dangers the diabetic may encounter; the use and abuse of the various types of insulin, the dangers of insulin shock, coma and gangrene following trauma.

On page 67, the physician will find interesting statements regarding the contemplated marriage of diabetic patients and the transmission of the disease to the children and their children.

The reviewer recommends translation into several languages, so that diabetics may read and benefit from the advice given by Professor Bertram.

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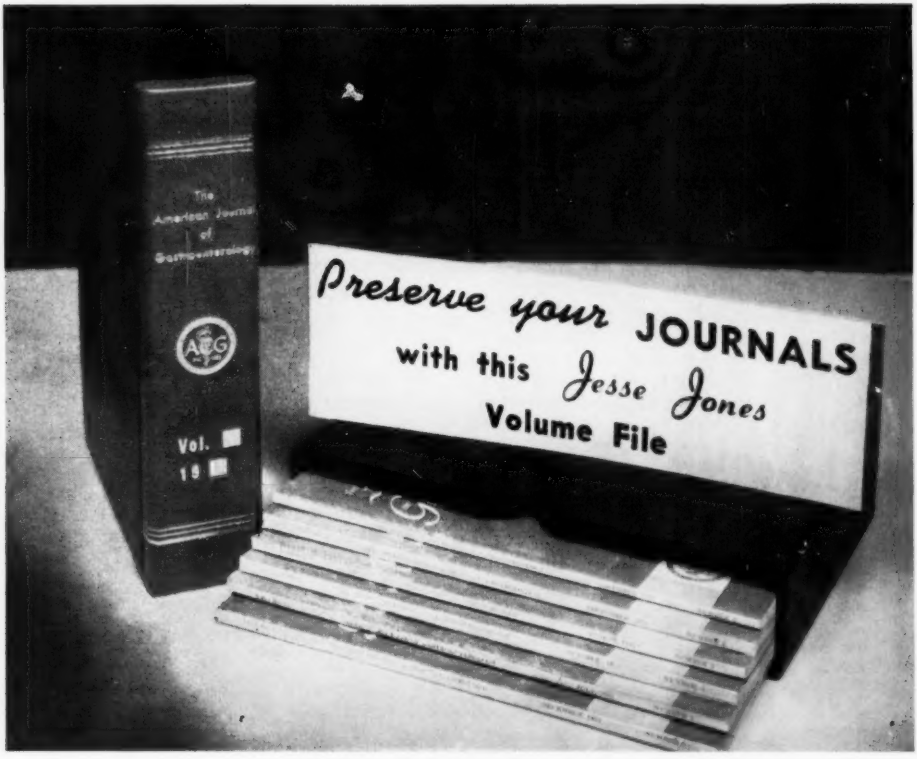

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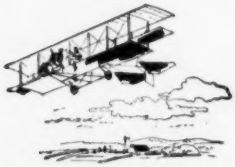
The bride wore goggles



ON OCTOBER 26, 1912, an ungainly biplane swooped into a Michigan pasture like an overfed duck and promptly nosed over on its back. Its contents proved to be a teen-age couple who got married as soon as they regained consciousness.

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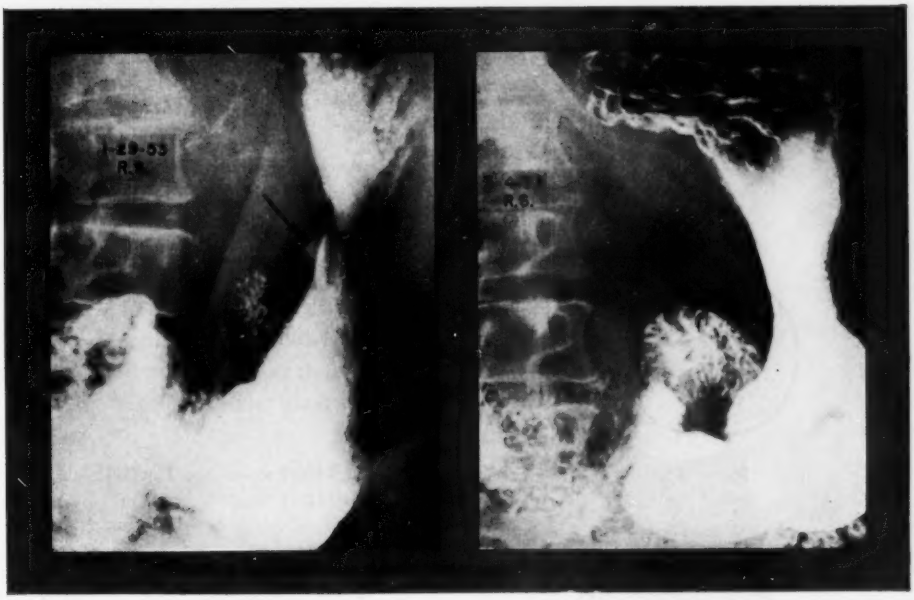

Antrenyl is a potent, dependable anticholinergic agent which not only relieves ulcer symptoms, but has been shown to exhibit a definite deterrent action upon the development of ulcers in the Shay rat.[1]

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1. Barrett, W. E., Rutledge, R., Plummer, A. J., and Yonkman, F. F.: J. Pharmacol. & Exper. Therap. *108*:305 (July) 1953. 2. Rogers, M. P., and Gray, C. L.: Am. J. Digest. Dis. *19*:180 (June) 1952.

Supplied:
TABLETS, 5 mg. (white, scored); bottles of 100, 500 and 1000.
SYRUP, 5 mg. per 4-ml. teaspoon; bottles of 1 pint.

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2/2294M

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- prolongs remissions, curbs recurrences
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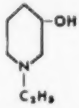
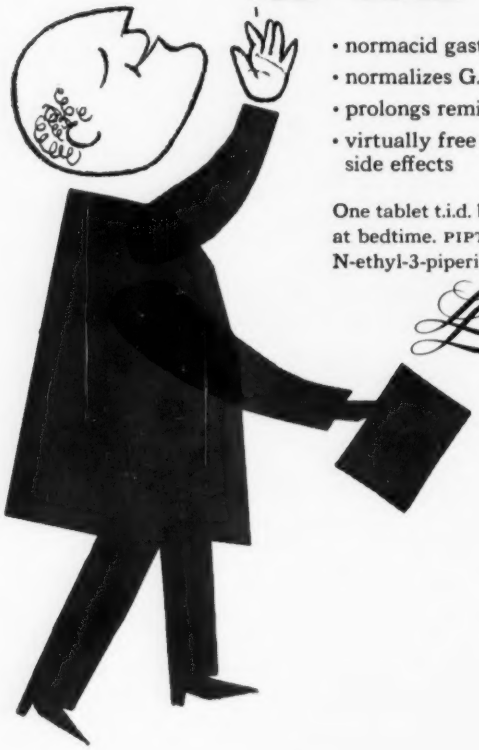


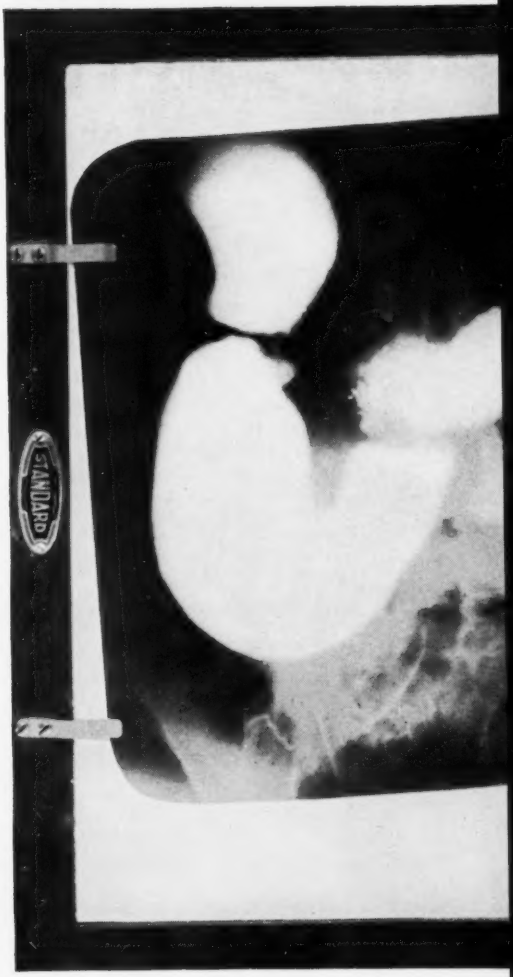


. . . part of *every illness*

ANXIETY

is part of

PEPTIC ULCER



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Non-sensitizing, non-irritant Desitin Ointment combines high grade Norwegian cod liver oil, zinc oxide, talcum, petrolatum and lanolin. Tubes of 1 oz., 2 oz., 4 oz., and 1 lb. jars.

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1. Grayzel, H. G., Heimer, C. B., and Grayzel, R. W.: New York St. J. Med. 53:2233, 1953. **2.** Heimer, C. B., Grayzel, H. G., and Kramer, B.: Archives of Pediatrics 68:382, 1951. **3.** Behrman, H. T., Combes, F. C., Bobroff, A., and Leviticus, R.: Ind. Med. & Surgery 18:512, 1949. **4.** Turell, R.: New York St. J. Med. 50:2282, 1950. **5.** Marks, M. M.: Missouri Med. 52:187, 1955.

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